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SUMMARY OF RECENT ABSTRACTS*

VI. PLAGUE

Epidemiology: Rodent Plague

Plague occurred in Malta (and in N. Africa, Egypt, Palestine, Italy, Sicily, Rhodes and Corsica) in 1945, and CAUCHI (p. 784) reports that there were 80 cases with 22 deaths. Infected rats were detected until early 1947, but not since. In this outbreak in Malta, during the year, 22,902 rats were examined, most of which were *R. norvegicus*. BARNETT (p. 998) found plague in 20 of them, of which 15 were *R. norvegicus*. This is evidently the important rat in relation to plague. Zinc phosphide, arsenious oxide, red squill and ANTU were used against the rats.

ERZIN and PAYZIN (p. 426) report an outbreak of plague in Turkey. They treated their cases with sulphonamides and serum, with success.

GIRARD (p. 595) points out that the term sylvatic plague is a misnomer in that the rodents inhabit not forest land but steppe country. He claims that all plague in N. Africa, French W. Africa, Madagascar, the Netherlands Indies and in India, whether in towns, villages or hamlets, is murine, and the only reservoir is the domestic rat. Elsewhere, other rodents are involved, and plague rodents may therefore be distinguished as wild or domestic.

HOPKINS (p. 995) thinks that plague has been present in Uganda from ancient times, latent but never absent. There is no sylvatic plague, and the rodent reservoir comprises *Rattus rattus* (previously *R. (mastomys) coucha ugandae* which has now been supplanted by *R. rattus*). *Xenopsylla brasiliensis* is the chief vector though *X. cheopis* is present. For epidemics to occur there must, of course, be intimate contact between rats and man (and the rats are climbers, nesting in thatch or iron roofs); the average rainfall has always been about 45 inches in times of epidemics in Uganda. In the Léopoldville area of the Belgian Congo, WANSON *et al.* (p. 425) found *R. rattus* and some of its varieties, but no *R. norvegicus*; 22 species of non-domestic rodents have been recognized. Of the fleas, *X. brasiliensis* was the most common on rats, but *X. cheopis* was also very abundant. These are rarely seen in houses. Only 1 per cent. of the field rodents carried fleas, *X. nubicus*, *X. brasiliensis* and *X. cheopis*. The authors give much information on the rodents and their habits, and on the other ectoparasites found on them.

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1948, v. 45. References to the abstracts are given under the names of the authors quoted, and the pages on which the abstracts are printed.

The history of plague in the Americas is reviewed by FAUST (p. 426), and by HOEKENGA (p. 171), who comments on the chronic or latent infection found in rodents and on the long period of infectivity of fleas (exceptionally up to 396 days). For control in the face of epidemics, the use of DDT, together with the rat poison sodium fluoracetate (" 1080 ") is desirable. Immunization with a killed vaccine of organisms grown at room temperature is practised.

In the United States the known area of infection of field animals with plague was extended in 1946 by the discovery of the disease in a prairie dog and in a pool of fleas from these animals (*Public Health Reports*, p. 171). In the same journal (p. 513) it is recorded that plague was found in a pool of fleas from Dawson County, Texas. The fleas were collected from pack rats (*Neotoma micropus*). In *Public Health Reports* (p. 1082) an account is given of a fatal human case of plague in California, the first natural infection to be reported in U.S.A. since 1943. In 1947 rodent plague was recorded from six western States.

BARRETO & DE CASTRO (p. 171) sum up the epidemiology of plague in Brazil. When it was first introduced, in 1899, it was a disease of the chief ports ; in the next period it passed to the cities of the interior ; and in the third period, which continues to the present time, it is tending to disappear from the cities and to localize itself endemically in rural zones. It is associated with the storage of various crops in the houses of the people, and these crops attract rodents. The principal vector is *X. cheopis*, except in São Paulo (temperate zone) where *X. brasiliensis* is more important. Plague tends to increase in spring and autumn, after the periods of heaviest rainfall, with temperatures between 19° and 26°C., and relative humidity between 66 and 83 per cent. For diagnosis, haemoculture and intraperitoneal inoculation of guineapigs are advocated, but gland puncture is not approved ; for post mortem diagnosis the bone marrow from amputated digits is used. For treatment sulphadiazine is recommended ; penicillin has been discarded.

Transmission

LIMA and HATHAWAY (p. 173) have compiled a very extensive bibliography of fleas and their animal hosts, and a catalogue of the fleas of the world, and of the animal hosts. This publication will be most useful as a work of reference. CHABAUD (p. 994) has compiled a comprehensive list of rodents and fleas concerned in sylvatic plague, and in plague of domestic rodents and man. He recognizes the fact that all the Siphonaptera can become infected, and has never found any species of fleas incapable of transmission if they were numerous and acting on a preferred host.

BURROUGHS (p. 254) has calculated the vector efficiency of several species of fleas, and compared them with *Xenopsylla cheopis*. Efficiency is expressed numerically, the number being calculated according to a formula which takes into account various relevant factors. *X. cheopis* was the most efficient of the fleas studied, followed by *Nosopsyllus fasciatus* and others, but *Diamanus montanus* showed only low efficiency, which may have been a peculiarity of the particular strain used. Transmission by blocked fleas is most important, but mechanical transmission is also important in epizootics.

SHARIF (p. 596) has studied the nutritional requirements of flea larvae. Usually they live on decaying organic matter containing micro-organisms, and their principal requirements are proteins and vitamins. The ideal diet is dried blood and yeast ; blood and wheat flour, though it quickened larval development, was not a satisfactory diet for the larvae. The vitamins are probably derived from the association of micro-organisms with the food. *X. cheopis* and *X. brasiliensis* grow better than *X. astia* on flour alone, and this probably enables them to survive transport in grain, even without rats.

In his studies on the bionomics of *X. brasiliensis*, EDNEY (p. 332) records his findings on the factors which affect the longevity of adult fleas; for details the original should be consulted.

In Saigon HÉRIVAUX and TOUMANOFF (p. 596) observed an outbreak in man although the *X. cheopis* index for rats did not rise to the level of 5 per rat, usually regarded as the danger point. This was the predominant flea, but there was no correlation between the index and the course of the epidemic. TOUMANOFF and HÉRIVAUX (p. 995) draw attention to the well-known fact that the microclimate in which fleas exist may be very different from the climate outside. They found that the soil and refuse in which *X. cheopis* flourished were different from those where *X. astia* was found; the former soil was sandy clay, retentive of water, the latter was sandy. It is known that the temperature requirements of *X. cheopis* are lower than of *X. astia*, and the differences in soil environments may be a reflection of the fact that evaporation of water leads to lowering of temperature.

In a discussion of the part played by *Pulex irritans* in the transmission of plague, SWELLENGREBEL (p. 74) makes the point that even if it is eventually proved that transmission by this human flea is important in any place, this should not lead one to under-rate the primary importance of measures directed against that part of the murine population which is living in close contact with man.

HOPKINS (p. 255) has published a key to the known fleas of East Africa.

Aetiology

There is still argument about the identity of *P. pestis* and *P. pseudotuberculosis*, and some workers think that the latter is a variant of the former. GIRARD (p. 173) does not hold this view, but admits that bacilli from sylvatic plague differ from those of murine plague in that they acidify glycerin, and he thinks that under the influence of phage there might be further change in the direction of *P. pseudotuberculosis*. He holds that extracts of plague bacilli are toxic for rats and mice, whereas extracts of *P. pseudotuberculosis* are not, and suggests that this test may be used to clarify the position. ARAUJO COSTA (p. 513) has written a monograph on the diagnosis of plague in rats. He deals with the methods of differentiating *P. pestis* from other species of *Pasteurella*, especially *P. pseudotuberculosis*, and he strongly advocates the examination of bone marrow of decomposed animals.

SANDOR *et al.* (p. 994) produce additional evidence to show that the antigens of *P. pestis* are not exotoxins or true toxins, but are bacterial antigens. Plague antiserum is of the antibacterial, not of the antitoxic, type.

Clinical Findings: Treatment

MEYERS (p. 174) discusses diagnostic difficulties in plague.

WYNNE-GRIFFITH (p. 704) reports an outbreak of pneumonic plague in Rangoon. He does not think that this form of plague is particularly infectious in certain circumstances, the incubation period is short and there is a non-infectious phase for 24–48 hours after clinical onset. Immediate isolation should abort an outbreak.

MANI (p. 74) sums up much work on chemotherapy with sulphathiazole and sulphadiazine, and discusses a broth vaccine used successfully during the war.

In a large series of cases treated with sulphonamides WAGLE and COLAH (p. 256) found that the best prognosis was in patients with leucocyte counts within normal limits. The degree of septicaemia, calculated on colony counts of blood sown on agar, is the main factor in determining severity, and the fatality rate rises as the colony count rises.

SIMEONS and CHHATRE (p. 332) have treated plague patients with sulphamerazine, in various schedules, and have found that a course of 3 injections (2·5 gm., 1 gm. and 1 gm.) at intervals of 8 hours, followed by oral administration of 1 gm. every 8 hours, is about as effective as a course of sulphadiazine given every 4 hours. They therefore advocate this course of sulphamerazine because the 8-hour intervals are more satisfactory than the 4-hour intervals. For control of epidemics they rely on DDT. The use of cyanogas and kerosene-soap emulsion, formerly advocated, is not now advised since it kills off the rats but has no effect on the fleas, and is often followed by a sudden rise in incidence of the disease.

TIEH *et al.* (p. 512) report three recoveries in patients with primary pneumonic plague treated with sulphadiazine, and they also report that virulent *P. pestis* were found in throat swabs from 4 of 42 symptomless contacts so examined. The organisms persisted for 6–15 days, and at least one of these persons was regarded as a true healthy carrier.

HUANG *et al.* (p. 996) report a case of pneumonic plague, presumably contracted in a laboratory, in which cure was effected by streptomycin and sulphadiazine, with transfusions and administration of oxygen. Contacts were given sulphadiazine and none developed the disease.

A preliminary report by KARAMCHANDI and RAO (p. 333) on the use of streptomycin in a small number of cases of plague, is very favourable. HADDAD and VALERO (p. 784) report dramatic success with streptomycin in three cases of bubonic plague which were not responding to sulphonamides and penicillin. QUAN *et al.* (p. 597) find that streptomycin is the most effective therapeutic agent yet discovered for the treatment of all forms of plague in mice and guineapigs, and they suggest that it should be given early in human plague—2 gm. daily in bubonic, and 4–6 gm. daily in septicaemic and pneumonic infections—together with antiplague serum if there is profound toxaemia. MEYER *et al.* (p. 997) show that after intranasal instillation of virulent *P. pestis* in suspension in mice and guineapigs there develops a primary pneumonia, like that seen in man. Immunization with avirulent or chemically killed *P. pestis* confers marked protection, and concentrated antiplague serum protects and has some curative action. Sulphonamides are not very effective in pneumonic plague unless used with serum; streptomycin is the most effective therapeutic agent known. For human pneumonic plague daily doses of 4–6 gm. streptomycin should be given early and continued for 6–10 days.

Immunization: Control

MEYER and FOSTER (p. 896) show that agglutinin tests, complement-fixation tests and whole blood tests have proved inadequate to assess the immunity provoked by inoculation of plague bacilli, and they have applied a mouse protection test, with the serum of inoculated persons, to this subject. When the death rates and the survival times of the mice are taken into account, it appears that inoculation with a purified fraction antigen produces good antibody formation, that formalin-killed bacilli and one strain of living avirulent organisms are much less effective, and that the famous Tjiwidej strain, as used in this experiment, is not immunogenic. Adequate protection requires reinoculation with booster doses.

In control of outbreaks in Haifa POLLOCK (p. 597) relied on residual DDT spray for buildings, DDT dusting powder for personal use, and treatment with sulphadiazine and streptomycin. More permanent anti-rat measures are taken when possible, but the immediate measures outlined offer the best means of quick control.

Within a week of the application of 5 per cent. DDT powder to rat burrows and runs in shops, warehouses etc. in S. Carolina, the fleas were almost

completely eliminated from rats. NICHOLSON and GAINES (p. 598) could not detect any significant degree of recovery on the part of the flea population three months later, and there was no better result from the use of 10 per cent. DDT powder. *Charles Wilcocks*

MALARIA

BEDFORD, P. D. **Persistent Malarial Infestation in Fully Mepacrinised Troops.** [Correspondence.] *Lancet.* 1949, Apr. 9, 627.

This correspondent refers to the possible reservoirs of malaria among parasitized ex-Servicemen returning to temperate zones after service in the Tropics. While serving in the R.A.F. he decided, in attempting to compute the magnitude of the potential reservoir, that a minimal estimate could be formed from the number of healthy servicemen without a history of malaria who had been on regular suppressive mepacrine, but who harboured parasites in the peripheral blood. Such men, on returning to Britain " would escape the blood examinations normally carried out on those with a history of overt malaria."

In late 1945, he selected 100 airmen all of whom fulfilled the following criteria :—

(1) They had spent at least a year in the Far East under primitive conditions in hyperendemic malarious zones.

(2) All had been taking 0·1 gm. suppressive mepacrine for at least a year and had appeared to have absorbed it.

(3) None had had a major illness nor a history nor evidence of malaria, proved or " clinical " in the past year.

(4) All were fit at the time of sampling and had been in an area of low endemicity for over three months of the cool season : they were " due for home " in a few months.

Thick blood films stained by Field's method showed that five of the hundred men had *P. vivax* gametocytes in the blood.

The author discusses the future epidemiological significance of this finding, bearing in mind that latent malaria may declare itself after an incubation period of many months : and he suggests that, even though indigenous malaria arising from returned servicemen is negligible up to now, " the detection and cure of even 5 per cent. of healthy ' carriers ' may well be considered as a rational public-health procedure " should the position change at some future date. *H. J. O'D. Burke-Gaffney*

ZANETTI, V. & LAMBRECHT, F. L. Notes sur la malaria indigène au Nepoko. [**Indigenous Malaria in Nepoko.**] *Ann. Soc. Belge de Méd. Trop.* 1948, Sept. 30, v. 28, No. 3, 355–70.

The Nepoko Valley is in the Stanleyville Province, Belgian Congo, 2° 30′N, at an altitude of 800 metres. Rainfall is abundant, 2,000 mm. a year. November to January, inclusive, is a relatively dry season, as are two or three weeks in July—August. Anopheline density is low ; *A. gambiae* occurs. The population is agricultural ; there are no large centres of population.

The blood was examined of 1,562 persons, of both sexes and all ages, attending three rural dispensaries for any reason, between April and December. Malaria parasites were found in 547, 35 per cent., all *P. falciparum* : crescents were found only eight times. These 1,562 included a certain number of patients seeking treatment for acute malaria.

During the same period, the blood of 160 women admitted to the Maternity Hospital at Pawa was examined: 36 harboured malaria parasites, for the most part very few in number.

Other observations confirm the fact that the parasite index in this region is low compared with other parts of the Belgian Congo. Clinically malaria is a mild disease among adults, but may be very severe among infants. It is a very important cause of infant mortality.

Paludrine has been used both for treatment and prophylaxis. For treatment children from 1 to 3 years were given 0·05 gm. a day, older children 0·1 gm. a day, and adults 0·3 gm. a day for 10 days. Against schizonts the action of the drug was rapid and potent; against gametocytes, negligible. In 4 cases mature schizonts of *P. malariae* appeared in the blood during the first week of treatment and after *P. falciparum* had disappeared. Paludrine was less effective against the sexual forms of *P. falciparum* and against *P. malariae* than either quinine or atebrin [mepacrine], though very effective against *P. falciparum* schizonts. It rapidly reduced splenomegaly.

In examining the blood of 1,873 persons of all ages the authors found microfilariae of *Acanthocheilonema perstans* in 927, 49·5 per cent., and of *Loa loa* in 230, 12·3 per cent. *A. perstans* was found in 3 and *Loa loa* in 2 of 112 infants whose blood was examined during the first five days of life.

Norman White

SWELLENGREBEL, N. H. & SWELLENGREBEL, J. M. H. Malariabesmetting in de opeenvolgende leeftijdsklassen ener autochthone bevolking in hoog-endemische malariastreken der N.O.-kust van Nieuw-Guinea. [**Malaria Infection in Successive Age-Groups among the Indigenous People in Hyperendemic Malarious Areas in the North-East Coast of New Guinea.**] *Nederl. Tijdschr. v. Geneesk.* 1948, Oct. 30, v. 92 (iv), No. 44, 3498–504, 4 graphs. English summary.

The human response to hyperendemic malaria is compared as it occurs in Sumatra, S. Africa, Surinam and New Guinea. The West Indonesian form is characterized by uniform high spleen rates in all age groups, while the high parasite rates in young children diminish with advancing years. The African form is characterized by high spleen rates in young children and lower ones in adults, and this is combined with parasite rates which in children are double and in adults treble the W. Indonesian rates. On the other hand, the natives of hyperendemic areas in New Guinea show a parasitic response which closely approaches the African type and a splenic response which is intermediate between it and the W. Indonesian type. There is a gradual but not a fundamental difference between the two types. This difference is best explained not so much by racial peculiarities as by the rising immunity resulting from increasing rate of infection; this, in turn, tends to diminish splenic reaction.

P. Manson-Bahr

YAO, Y. T. **Synopsis of the Epidemiology of Important Parasitic Diseases in China. Part I. Malaria, with Keys to the Chinese Anopheline Mosquitoes.** *Chinese Med. J.* Chengtu Edition. 1945, Apr., v. 63A, No. 3, 103–26. [Numerous refs.]

This summarized information was put together for the benefit of Chinese and foreign medical members of armed forces in China. Of parasitic diseases malaria, kala azar, schistosomiasis and hookworm infection are of the greatest importance to China. Part I of the synopsis deals only with malaria.

Malaria is widespread in China. *P. vivax* and *P. malariae* infections occur all over the country; *P. falciparum* infections are only found south of 35°N

where they are most prevalent in hilly regions. Endemic malaria throughout the country is predominantly due to *P. vivax*. A summary of the salient results of numerous malaria surveys in different parts of the country is presented in tabular form. Blackwater fever is relatively common in Yunnan and Hainan Island ; elsewhere it is very rare.

Thirty-seven species and varieties of *Anopheles* have been identified in China ; these are listed with notes on geographical distribution of each. Seven species have been incriminated as vectors : *A. minimus*, *A. jeyporiensis candidiensis*, *A. maculatus*, *A. hyrcanus sinensis*, *A. pattoni*, *A. maculipennis atroparvus*, and *A. sacharovi*. In hilly regions of the south, *A. minimus* and *A. candidiensis* are the most important vectors. In hilly regions of the north, *A. pattoni* is probably an important carrier. *A. sinensis* is the chief vector throughout the plains of China. *A. atroparvus* is of local importance in Heilungkiang in the north-east and *A. sacharovi* in Sinkiang in the north-west.

Keys are annexed to facilitate the identification of both adults and larvae of all species hitherto reported from China. *Norman White*

FAUST, E. C. & HEMPHILL, Faye M. **Malaria Mortality and Morbidity in the United States for the Year 1946.** *J. National Malaria Soc.* 1948, Dec., v. 7, No. 4, 285–92, 3 figs. (folding maps).

This is a yearly statistical analysis of the incidence of malaria in the U.S.A., illustrated by detailed tables and maps showing the morbidity and mortality in each State, for information on which it must be consulted in the original.

Between 1931 and 1938 malaria incidence increased considerably, and towards the end of the war returning soldiers provided many exogenous cases as well as a parasite reservoir from which others became infected, and about this time DDT came into use. Diagnosis has also improved. The effect of each of these factors cannot be disentangled from the total picture which shows a decrease in reported deaths from a maximum of 4,678 in 1933 to 341 in 1946, and in reported cases from 136,433 in 1935 to 47,903 in 1946. The authors have some critical comment on the reliability of data. They conclude that malaria is steadily declining, and in formerly hyperendemic areas is changing from an acute to a mildly chronic, essentially quiescent form.

G. Macdonald

WEYER, F. Die "Rassen" von *Anopheles maculipennis* in Deutschland. [**The "Races" of *Anopheles maculipennis* in Germany.**] Reprinted from *Ztschr. f. Parasitenk.* 1948, v. 14, 38–59, 17 figs. [13 refs.]

Only *A. maculipennis atroparvus*, *A. m. messeae* and *A. m. typicus* occur in Germany. This paper first recapitulates the well-known problem of the morphological differentiation of these races and, in addition to the textual descriptions of the various stages of the mosquito, gives figures of the male claspettes, the larval head, palmate hairs, and thirteen photographs of the diagnostically important egg patterns. It then goes on to outline the geographical distribution and biological characteristics of the three races.

A. m. atroparvus is primarily a coastal species breeding in brackish water, its eastern limit being Frische Haff. It occurs, however, 30–60 kilometres inland along river courses, *e.g.*, the Elbe, and has been found as far inland as near Bochum and Paderborn in Westphalia, Hümmling in Emsland, Bad Oldesloe and Bad Sülze in Mecklenburg ; also near Eisleben, Magdeburg and

Goslar, and in East Germany and the Black Forest. In inland regions the water may be fresh or salt. It breeds in animal watering ponds, weedy stagnant ditches, swampy pools, drains and often in small open pools with limited vegetational growth. Precipitin tests have shown *atroparvus* to feed on pig, horse, cattle, goats, sheep, rabbits, and less frequently on man, in nature, but it will feed on man readily in captivity. The adults are found in spring and summer in stables, cattle-sheds, pigstyes, rabbit hutches, sheep and goat sheds but not in fowl houses or kennels. During hibernation they rest mainly in lofts, barns and empty outhouses but some are to be found in occupied animal sheds. These are *atroparvus* females which, since hibernation is only partial, have recently fed on the stalled animals. *A. maculipennis* females resting in occupied animal sheds in winter are always *atroparvus*. Hibernation extends from September until the end of March. Winter blood meals require, at 20°C., 2–3 days for digestion and 15–20 meals are required under experimental conditions for egg production.

A. m. messeae is the commonest race in Germany and is essentially an inland, freshwater, breeder. It is the only race occurring along the East Prussian coast, but the salinity of the breeding places there is not certainly known. It breeds in low-lying marshy areas, in ditches, in standing water along the course of rivers, or in the weedy edges of lakes. It occurs, for example, in the lake districts of Mecklenburg and of Upper Bavaria, at Lake Constance, and along the valleys of the Oder, Weser, Elbe, Rhine, Danube and Neckar rivers. The adults are found in summer in stables and cattlesheds, less usually in pigstyes, and it is frequent in fowl houses and kennels. It hibernates completely and in the same type of resting places as *atroparvus*, except in stalls actually occupied by animals. *A. m. messeae* does not feed readily on man or rabbits in the laboratory but will do so on fowls. A high percentage contain bird blood in nature, possibly of water fowls.

A. m. typicus is not found in the north sea-coast region of Germany. It is the least common of the three races and, although essentially a mountain race occurring in the Harz Mountains and the Black Forest, is known from Mecklenburg, Westphalia and near Magdeburg and Goslar. It is sometimes found in the same breeding places as *atroparvus* and *messeae*; in the Black Forest it is known from mill ponds constantly refreshed by the cool water of mountain streams. Nothing is known of its host preferences but it is found in cattlesheds in the Black Forest. Its hibernation habits are thought to be similar to those of *messeae*.

A. m. atroparvus is stenogamous, *messeae* and *typicus* are eurygamous. A section records briefly the varying degrees of fertility between the races none of which when crossed are known to be capable of producing fertile progeny.

This paper contains nothing that is new concerning the biology or morphology of these races. It is a useful summary of the subject in view of the remarkable increase in the incidence of malaria in Germany since the recent war [this *Bulletin*, 1948, v. 45, 1050]. The author states that the recent incidence of malaria in Germany is not due to a close association of overwintering *atroparvus* with the human population as occurs in Holland but that transmission in such places as Berlin, Brandenburg, in Württemberg and in the Rhineland is by *messeae*. [In the reference quoted, the same author reports that many new mosquito breeding places have appeared in German towns as a result of war-time destruction, *e.g.*, in neglected ruins, bomb craters, in neglected ornamental ponds and parks, and as a result of breached dams and river banks or the blockage of water courses. In one year more than 800 anopheline breeding places were reported in Berlin. Neither paper, however, gives sporozoite indices incriminating *messeae* as the vector in the recent outbreaks of malaria in Germany.] *D. S. Bertram*

WHITE, R. Senior. **Malaria Transmission in the Light of Modern Evolutionary Theory applied to Malaria-carrying Mosquitoes.** *Indian J. Malariology.* 1948, Mar.–June, v. 2, Nos. 1/2, 13–33. [34 refs.]

The author points out that even within the limits of Asiatic *Anopheles* there are several species which transmit malaria in a part of the area but not elsewhere : *A. sundaicus* may cause an outbreak of malaria in a certain place, but at other times transmit the disease very rarely. Other small but constant differences exist within the limits of a species in the conventional sense. These and many other facts point to the existence of units of less than specific rank differing mainly in physiological characters [though it might be added, one must be cautious in considering the facts, some of which might be due to changes in the environment].

In considering these matters the author has been much stimulated by reading *Evolution—the Modern Synthesis* by Julian HUXLEY (1942). In this paper he makes extracts from that book, calling attention to the large number of similar cases which are recorded from other groups of insects. For instance, within a species there may be separate races which are adapted to different foods ; there are what one might call psychological differences which reduce the cross-mating between groups within one species. The question of the distribution and spread of mutations through a population is also considered. Huxley has also called attention to that interesting phenomenon, the development of races of insects resistant to insecticides. The evidence seems to show that in certain scale insects and in codling moths a strain resistant to cyanide fumigation has been produced, which is also abnormally resistant to other toxic substances to which it has not been exposed. This phenomenon of a development of general rather than specific resistance is difficult to understand and, in Senior White's view, fundamental. He feels that before so very long we shall be forced to abandon the use of insecticides, even the most powerful, and that we shall achieve control to a great extent by the use of biological methods. The entomologist who has recently felt that his job may vanish because of the activities of the organic chemist will take courage.

The paper is full of interesting material and ideas : we have found it difficult to summarize. The author's conclusion is that there is a call " for investigators who will apply and extend the methods of pure zoological research to the problem of biological mosquito control ". *P. A. Buxton*

DE GAETANI, G. F. Patogenesi della malaria. Stato attuale delle ricerche. [**Present Knowledge of the Pathogenesis of Malaria.**] 58 pp., 1 coloured pl. [Bibliography.] Reprinted from *Atti Accad. Sci. di Ferrara.* 1946.

A general review.

TAYLOR, H. L., MICKELSEN, O. & KEYS, A. **The Effects of Induced Malaria, Acute Starvation and Semi-Starvation on the Electrophoretic Diagram of the Serum Proteins of Normal Young Men.** *J. Clin. Investigation.* 1949, Mar., v. 28, No. 2, 273–81, 1 fig. [31 refs.]

v. HALLER, E. Die Erkrankungsdauer der Malaria (insbesondere der Malaria tertiana). [**The Duration of Malaria, especially *P. vivax* Infections.**] *Ztschr. f. Hyg. u. Infektionskr.* 1948, v. 128, Nos. 3/4, 379–87, 1 fig. [25 refs.]

These original observations were made from June to September 1945 in a prisoner of war camp at Rimini on the Adriatic and appeared to show that 1½ years from the last infection no further relapses occurred and that all risk

of sequelae had then ceased to exist. The material consisted of 1,262 soldiers originally infected in Sardinia; the majority had suffered from relapses (in the region of 60 per cent.). They had left Sardinia in September 1943. Without going into details the author feels justified in concluding that the duration of infection in tertian malaria seldom oversteps the two-year limit, but usually no symptoms are manifested after 1½ years. That this is due to the disappearance of the parasite is suggested by the fact that it occurs before immunity is produced and while the patient is still susceptible to a fresh infection. In direct contrast are the findings in therapeutic malaria produced by blood inoculation. Here relapses seldom, if ever, are noted after two months and only when the treatment has not been sufficiently vigorous. In the afebrile periods the blood is infective for mosquitoes while in the naturally contracted malaria this is not the case. In subtertian malaria relapses do not occur after a latent period of eight weeks and the infection seldom, if ever, persists for one year in the human body [see also this *Bulletin*, 1948, v. 45, 970].

P. Manson-Bahr

VAN DEN ENDE, H. Enkele gevallen van beenmergremming door malaria. [**Some Cases of Bone-Marrow Inhibition in Malaria.**] *Nederl. Tijdschr. v. Geneesk.* 1949, Jan. 15, v. 93 (i), No. 3, 163–9. English summary (4 lines).

Ten cases of varying degrees of bone-marrow inhibition in each of which malaria (usually *P. falciparum*) was commonly the only ascertainable factor. The anaemia was severe, accompanied by slight leucopenia and thrombocytopenia; megakaryocytes were also present. Malaria therapy was followed by great clinical and haematological improvement in each instance.

P. Manson-Bahr

ROBERTS, J. I. **Dysentery associated with Malaria.** *J. Trop. Med. & Hyg.* 1949, Apr., v. 52, No. 4, 76–8.

Further details are given of cases of dysentery occurring in the course of a malaria epidemic in Nairobi, Kenya, which was originally described by HEISCH [this *Bulletin*, 1941, v. 38, 230]. The dysentery was of a mild type, the stools not usually exceeding ten in 24 hours. Pus cells were rare in the stools, the blood was often bright red, but occasionally dark as the result of petechial haemorrhages in the intestinal mucosa. Malaria was believed to be the cause of the dysentery because (*a*) the condition responded very rapidly to quinine treatment, (*b*) malaria parasites were found in the peripheral blood and in blood contained in the stool, (*c*) the cases were associated with high fever and headache, and (*d*) dysentery organisms were rarely recovered from the faeces. The leucocyte count was generally within normal limits.

[These cases are unlike those of true intestinal malaria, a pernicious syndrome of *P. falciparum* malaria, which is much more severe and fatal, and shows developing and mature schizonts in the blood. In this series, rings and gametocytes only are reported.] *P. C. C. Garnham*

VAN STEENIS, P. B. Enkele opmerkingen over de behandeling van malaria. [**Observations on the Treatment of Malaria.**] *Nederl. Tijdschr. v. Geneesk.* 1948, Dec. 11, v. 92 (iv), No. 50, 4084–92. English summary (5 lines).

In persons who have been repatriated from Indonesia malarial relapses are caused by the benign tertian parasite. In the question of appropriate treatment the whole problem of malaria therapy is discussed and it is concluded that the

best course of treatment to prevent relapses is a combination of quinine and pamaquin in a series of short courses of low dosage. The problem of nutrition is also important. *P. Manson-Bahr*

Dreisbach, R. H. **Antagonists for Fatal and Non-Fatal Doses of Quinine intravenously in Depressed Circulatory States and in Hyperthermia.** *J. Pharm. & Exper. Therap.* 1949, Mar., v. 95, No. 3, 347–51.

Moe, G. K., Peralta, B. & Seevers, M. H. **Central Impairment of Sympathetic Reflexes by 8-Amino-quinolines.** *J. Pharm. & Exper. Therap.* 1949, Mar., v. 95, No. 3, 407–14, 2 figs.

"1. Pamaquine, pentaquine, and isopentaquine chronically administered to dogs produce impairment of sympathetic cardiovascular reflexes, but not of parasympathetic or respiratory reflexes.

"2. Pentaquine and isopentaquine, but probably not pamaquine, cause similar effects in the monkey.

"3. The impairment of reflexes is believed to be due to destruction of medullary cell-groups."

Colette, Mlle. & Porot, M. Les psychoses quinacriniques. [**Psychoses attributable to Quinacrine.**] *Algérie Med.* 1948, Aug.–Sept., No. 7, 375–86. [15 refs.]

The authors describe nine cases which came under their personal observation within a period of one year in which the patients developed acute mental derangement after the administration of quinacrine [mepacrine] in therapeutic doses. Five of the patients had a history of some form of mental trouble in the past, melancholia, short or prolonged confusional states, anorexia nervosa or the like. In six of the nine cases malaria could be definitely excluded as a possible contributory cause of the mental derangement. The onset of mental symptoms occurred very shortly after quinacrine treatment, within a week at most, except in one case where mental symptoms did not appear till one month after the ingestion of 3·5 gm. of the drug.

All the patients had maniacal symptoms, accompanied in some cases by a confusional state, often by an anxiety state, at times intense, and sometimes by very painful hallucinations. The symptoms lasted for one to six months except in two cases in which mental symptoms were of only two and ten days' duration, respectively. The ultimate prognosis is good in all cases. There is no specific treatment. Six cases were treated by electro-shock, the best method of calming maniacal agitation. In one case insulin coma was used with success.

The authors consider that quinacrine should be avoided in the treatment of patients with a history of past psychosis, or of patients in a state of mental disequilibrium. A warning is also given against a too hasty diagnosis of malaria, on insufficient grounds. *Norman White*

Guija Morales, E. **Psicosis palúdicas y atebrínicas.**

This book is reviewed on p. 684.

Schmitt, C. L. **Present Status of Quinacrine (Atabrine) Dermatitis. Report of Six Cases.** *Arch. Dermat. & Syph.* 1949, Jan., v. 59, No. 1, 16–21.

The author distinguishes two distinct types of quinacrine [mepacrine] dermatitis: (1) The lichenoid type which is generally recognized, and (2) an

eczematoid type which he considers to be ten times as common. This second variety is characterized by patches of closely set, deep-seated miliary vesicles first appearing on the sides of the fingers, and subsequently affecting the wrists, and less frequently the feet, legs, ears, scalp, suprapubic region and scrotum. While the original eruption tends to heal, a recurrent eczematoid dermatitis may occur months or years afterwards. The recurrent dermatitis is similar in appearance to the original one, and may occur at previously affected sites or elsewhere. *H. T. H. Wilson*

Monthly Bull. Ministry of Health & Pub. Health Lab. Service (Directed by Med. Res. Council). 1949, May, v. 8, 92–4. **Recommendations on the Use of Paludrine (Proguanil) in Prophylaxis and Treatment of Malaria.** Also in *Brit. Med. J.* 1949, Apr. 2, 585–6 & *Lancet.* 1949, Apr. 2, 578–9.

"The following recommendations on the use of proguanil ('paludrine') in the prophylaxis and treatment of malaria, and suggestions for trial, are issued by the Colonial Office and the Medical Research Council on the advice of the Colonial Medical Research Committee. It should be clearly appreciated that the recommendations are tentative on the basis of present knowledge and that they are subject to review in the light of future experience and experiment.

Prophylactic Use

"The dose recommended for suppression of malaria of all types in endemic areas is 100 mg. daily. For children the following dosage is advised: from birth to 5 years—25 mg. daily; from 6 to 12 years—50 mg. daily. When a daily dose is not practicable one dose of 300 mg. should be taken on the same day each week; dosage for children should be in the proportion indicated.

"In the case of persons, other than the indigenous inhabitants, who have been resident in an endemic area for some time, or who have been otherwise already exposed to malarial infection, a full therapeutic course (see 1 (*a*) below) should be taken before entering on the suppressive regimen.

1. *P. falciparum* (Malignant Tertian) Infections; Mixed Infections; Undiagnosed Type Infections

"(*a*) *Treatment of Non-immunes.*—Proguanil alone cannot be relied upon to effect radical cure in all cases, and the clinical response with this drug unaided is also somewhat slow. It has been shown, however, that these disadvantages may be overcome by reinforcement with mepacrine on the first day of treatment. The following combined course is recommended *for trial*: 300 mg. proguanil twice daily for 10 days reinforced on the first day of treatment with three doses of 300 mg. mepacrine, and followed by 100 mg. proguanil daily for six weeks. (Persons continuing to live in an endemic area should continue their suppressive regimen.)

"(*b*) *Treatment of Clinical Attack in Semi-immune Subjects such as Labour Forces and Rural Populations in Endemic Areas.*—A single dose of 300 mg. proguanil will usually suffice to produce clinical cure. Relapses can be treated similarly as and when they arise. Serious cases should be given emergency treatment (see below).

"(*c*) *Treatment of Malarial 'Emergencies'.*—For treatment of conditions such as cerebral or algid malaria and where for any other reason the patient is unable to take drugs by mouth, immediate intramuscular mepacrine or intravenous quinine therapy should be employed.

2. *P. vivax* (Benign Tertian) Infections

"(*a*) *With the Object of Radical Cure.*—The course advised for adults is 100 mg. proguanil plus 10 mg. pamaquin base (or a corresponding dose of one

of the other 8-aminoquinoline derivatives) three times daily for 10 days. The dose for children should be proportionate. Pamaquin should not be given unless the patient can be kept in bed under medical supervision throughout the course; this is particularly important in the case of children. When the patient cannot be kept in bed the alternative course recommended is 100 mg. proguanil three times daily for 10 days followed by a single dose of 300 mg. proguanil on the same day each week for a year.

"(*b*) *Treatment of the Clinical Attack in Semi-immunes.*—As for M.T. malaria.

"Unless otherwise stated, the dosage mentioned is that for adults. In recommending the use of a single dose of 300 mg. proguanil for the treatment of the febrile attack in semi-immunes and a weekly dose of 300 mg. for suppressive purposes, the advantages of these procedures are emphasized as (*a*) bringing an effective antimalarial drug within the economic capacity of village and rural populations of endemic areas of malaria and (*b*) providing a method of prophylaxis easy of administration."

TERZIAN, L. A. & WEATHERSBY, A. B. **The Action of Antimalarial Drugs in Mosquitoes infected with** *Plasmodium falciparum.* *Amer. J. Trop. Med.* 1949, Jan., v. 29, No. 1, 19–22.

Since only those drugs which acted as prophylactics in the vertebrate host prevented oöcyst development in the mosquito, TERZIAN (this *Bulletin*, 1948, v. 45, 767] noted, from experimental evidence, that there was a correlation between drug action in the mosquito (*Aëdes aegypti*) infected with *P. gallinaceum* and in chickens infected with sporozoites of this parasite. The investigation has now been extended to *Anopheles quadrimaculatus* infected with *P. falciparum.* The earlier experiments with *P. gallinaceum* indicated that if sporozoites were present in the mosquito, they were always infective to the chicken host, and this has been accepted as a valid criterion of infectivity here, since it was not always practicable to test the point on human patients. The drugs used were added in sugar solution to the mosquito diet after they had fed on neurosyphilitic patients undergoing malarial therapy. Quinine, quinacrine [mepacrine], sontochin (SN 6911) and sodium sulphadiazine did not prevent oöcyst development or affect the production of sporozoites. Paludrine, however, prevented complete oöcyst development, although some partly developed forms were present when dissections were carried out on the fourth day after infection. Sporozoites were never present. Similar results have been recorded by FAIRLEY [this *Bulletin*, 1947, v. 44, 282]. The correlation noted above for *P. gallinaceum* thus appears to hold in the case of *P. falciparum.* This method of drug evaluation in the mosquito should be of value in screening prophylactic drugs in human malaria. *J. D. Fulton*

SEATON, D. R. & LOURIE, E. M. **Acquired Resistance to Proguanil (Paludrine) in** *Plasmodium vivax.* *Lancet.* 1949, Mar. 5, 394–5.

Experimental evidence of induced resistance to various drugs in malarial parasites of monkeys and birds has been provided in the last few years [this *Bulletin*, 1942, v. 39, 438; 1943, v. 40, 754; 1947, v. 44, 969, 970; 1948, v. 45, 48, 158]. The present investigation reports the production of resistance to paludrine (proguanil) in a strain of *P. vivax.* The patients were undergoing malarial therapy and the strain, which had not previously been in contact with paludrine, was maintained by blood inoculation. Two series of infected patients were treated with small doses of the drug. In the first series, 17 in number,

subinoculations from each patient were performed before drug treatment, while in the second series repeated small doses of paludrine were generally given before subinoculation from that patient. The minimum effective dose of drug which would terminate fever and parasitaemia within a fixed time was established as 1·25 mgm. daily on three consecutive days. Resistance to therapeutic doses became apparent only towards the end of the observation period of 20 months, during which 28 passages were made. At the end of that time it was approximately 80-fold in so far as three daily doses of 100 mgm. on successive days did not appear to influence fever or parasitaemia, although a dose three times as large did so. At the 23rd passage the strain was transmitted by mosquito and retained its resistant character. From their experience the authors conclude that there is little chance of producing resistant strains of the parasite by the clinical treatment usually employed. *J. D. Fulton*

Penido, H. M., de Sousa, E. F. & Bezerra, F. P. G., Jr. Estudo sobre a ação de novas drogas antimaláricas no Vale do Rio Doce. [**Study of the Activity of New Antimalarial Drugs in the Doce Valley.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1948, July, v. 2, No. 1, 23–36, 1 map. English summary (7 lines).

This preliminary study was designed to compare the efficacy of four new antimalarial drugs, each given in a single dose, in the treatment of acute attacks of malaria in patients living in eight localities in the valley of the Doce River. In many of these places cases of malaria were few in number; the houses had recently been sprayed with DDT.

The four drugs tested were camoquin, chloroquine, oxychloroquine and paludrine. For patients 15 years of age and over the dose of the drug administered was 1·0 gm. The total number of patients treated were camoquin 109; chloroquine 11; oxychloroquine 12; paludrine 33. Parasites were found in 87 of the patients, *P. falciparum* 43, *P. vivax* 37, *P. malariae* 4, mixed infection 3.

There were no symptoms of intolerance with any of the four drugs. Camoquin was very effective. Paludrine gave the poorest results. Of 12 patients treated with paludrine, 5 continued to show parasites in the peripheral blood 72 hours after the administration of the drug. These five patients were all in the age group 1–4; they had each received only 0·20 gm. paludrine. *Norman White*

Chaudhuri, R. N., Rai Chaudhuri, M. N. & Chakravarty, N. K. **Chloroquine (SN 7618) in Malaria.** *Indian J. Malariology.* 1948, Mar.–June, v. 2, Nos. 1/2, 1–12, 5 charts & 2 figs.

Fifty patients with active malarial infection were treated with chloroquine in the Carmichael Hospital, Calcutta. Eighteen had *P. falciparum*, 27 *P. vivax*, 1 *P. malariae*, and 4 mixed *P. vivax* and *P. falciparum* infections. The drug was given in tablet form, each tablet containing 0·25 gm. of the base. Some patients received two tablets as the first dose, another tablet after six hours and then one tablet on each of the two following days—five tablets in all. The remaining patients each received a single dose of six tablets. The above are doses for adults. The temperature fell to normal in an average period of 26·8 hours with the first treatment, and 24·9 hours with the second. Asexual parasites disappeared within 35 hours with the first treatment and 25·5 hours with the second. These results were more prompt than those obtained with either quinine, mepacrine or paludrine. Symptoms of toxicity were noted in 5 patients;

insomnia (4 cases), gastro-intestinal irritation (1 case), pruritus (3 cases), and pain in the lower abdomen, genitals and thighs (1 case). Gametocytes were apparently unaffected by treatment. *Norman White*

EJERCITO, A. & DUQUE, M. **Preliminary Report on Cam-AQI Dihydrochloride (Miaquin, Camoquin) in the Treatment of Human Malaria.** *J. Philippine Med. Ass.* 1948, Nov., v. 24, No. 11, 633–42.

This paper reports the results of the first trials of the treatment of malaria with CAM-AQI to be carried out in the Philippines. Each patient treated received a single curative dose, the main object of the inquiry being to determine the suitability of the drug for treatment of malaria in the field. Each adult patient received 8 tablets, 0·4 gm., of CAM-AQI. In all 128 patients were so treated, 84 with *P. vivax* and 44 with *P. falciparum* infections. *P. vivax* parasites and fever were absent on the 3rd or 4th day in most cases ; in afebrile cases the parasites had disappeared on the 2nd day. Fever in *P. falciparum* infections persisted from 3 to 5 days : schizonts disappeared from the blood in from 2 to 4 days. The drug had no apparent effect on crescents. No symptom of drug intolerance was ever noted. Only 9 of the *P. vivax* patients and 1 *P. falciparum* patient suffered relapse after treatment ; the periods of observation are not stated. *Norman White*

JANG, Chang-shaw. **Present Status of Studies on Chinese Antimalarial Drugs.** *Chinese Med. J.* Chengtu Edition. 1945, Apr., v. 63A, No. 3, 126–30.

Shortage of quinine and of synthetic malaria remedies during the war stimulated interest in indigenous remedies in China.

Sinine, an alkaloidal substance obtained from the root bark of an ash tree, *Fraxinus mallacophyla*, which grows in the south-west of Yunnan, was tried and found wanting. For centuries past the bark has been used as a febrifuge.

Fraxin, a glucoside obtained from the bark of *Fraxinus chinensis*, was tried in the treatment of eight patients with *P. vivax* malaria. The author found it to be devoid of antimalarial properties.

Ch'ang Shan has been credited with antimalarial properties for 4,000 years. The botanical identity of the original Ch'ang Shan appears to be a matter of some doubt. The name is now applied to a herb, *Dichroa febrifuga*. An extract containing water-soluble substances from the root was given to thirteen patients with *P. vivax* malaria. The results were stated to be comparable to those obtained with quinine in similar cases. Two alkaloids have been isolated from Ch'ang Shan ; further chemotherapeutic studies were being made [see also this *Bulletin*, 1948, v. 45, 755]. *Norman White*

GAGE, J. C. **Synthetic Antimalarials. Part XXXVI. Physicochemical Studies on Pyrimidine Derivatives.** *J. Chem. Soc.* 1949, Feb., 469–74, 3 figs.

ASHWORTH, R. de B., CROWTHER, A. F., CURD, F. H. S., HENDRY, J. A. RICHARDSON, D. N., Miss & ROSE, F. L. **Synthetic Antimalarials. Part XXXVII. Some N^1-p-Chlorophenyl-N^2 : N^4 : N^5-trialkyldiguanides and other Related Miscellaneous Diguanide Types.** *J. Chem. Soc.* 1949, Feb., 475–82.

DRAKE, N. L., HAYES, R. A., GARMAN, J. A., JOHNSON, R. B., KELLEY, G. W., MELAMED, S. & PECK, R. M. **Synthetic Antimalarials. Some Derivatives of 8-Aminoquinoline. II.** *J. Amer. Chem. Soc.* 1949, Feb., v. 71, No. 2, 455–8. [Refs. in footnotes.]

RAY, A. P. **Prophylactic Use of Paludrine in a Tea Estate.** *Indian J. Malariology.* 1948, Mar.–June, v. 2, Nos. 1/2, 35–66, 4 graphs. [17 refs.]

The observations recorded were made in a Tea Estate in a hyperendemic malarious region of North Bengal. The labour force numbered about 2,800, including 900 children. The vector is *A. minimus.* Prophylactic medication began on April 16 and was continued till October 29, 1947. A single weekly dose of paludrine, 3 tablets (0·3 gm.), was given to 538 persons ; 1 tablet (0·1 gm.) of paludrine was given twice weekly to 889 persons ; 1 tablet of chloroquine (0·25 gm. base) was given once a week to 292 persons.

There was a remarkable decline in the incidence of fever cases during the period of drug administration. The number of cases recorded from April to October in each of the years 1941 to 1947 was : *1941,* 1,974 ; *1942,* 2,064 ; *1943,* 3,022 ; *1944,* 2,834 ; *1945,* 3,818 ; *1946,* 2,794 ; *1947,* 158. Among the 158 cases of fever recorded in 1947 there were only 17 cases of proved malaria among 1,750 adults who had been placed on prophylactic treatment. Attendance registers showed that all but one of these 17 patients had taken the treatment irregularly. Only one case was considered to be a genuine " breakthrough ".

The total death rate for 1947 was 16·6 as compared with 32·77 per thousand for 1946. The birth rate in 1947 was 39·3 as compared with 13·8 per thousand in 1946, and the infant mortality rate 171·05 as compared with 260·4 per thousand live births in 1946. There was a marked improvement in the health and efficiency of the labour force. *Norman White*

KLOPPER, S., SLOP, D. & OP'T LAND, C. Een onderzoek naar de suppressieve werking van paludrine bij malaria tertiana. [**The Suppressive Action of Paludrine in Benign Tertian Malaria.**] *Nederl. Tijdschr. v. Geneesk.* 1948, Nov. 27, v. 92 (iv), No. 48, 3922–9, 4 figs. English summary (6 lines).

The effects of weekly paludrine therapy on the prevention of benign tertian malaria were investigated in a large number of persons. In doses of 100 mgm. a week for adults and 50 mgm. in children paludrine appeared to stave off the clinical attack. In persons with a tendency to relapse paludrine in these doses appeared to suppress such a relapse. *P. Manson-Bahr*

SMITH, H. F., DY, F. J. & CABRERA, D. J. **Studies on the Efficiency of Chloroquine and Chlorguanide as Antimalarials : I. As Suppressants.** Reprinted from *Acta Med. Philippina.* 1948, Oct.–Dec., v. 5, No. 2, 16 pp. [12 refs.]

This study of the relative suppressive value of two antimalarial drugs was carried out simultaneously in two places in the Philippines : among lumbermen and their families in an isolated valley 1,800 feet above sea-level in the Island of Luzon, and in a settlement on a plateau about 300 feet above sea-level in Negros Occidental. Both localities have well-defined wet and dry seasons and in both abundant streams are prolific breeding grounds for *A. minimus flavirostris,* the vector. Parasite and spleen surveys were made prior to the experiment. In both places the population was divided into three groups comparable to each other with regard to previous infection, spleen size, age and sex. Group I received chloroquine, Group II chlorguanide (paludrine), Group III received sodium bicarbonate as a placebo. Adults were each given two 0·25 gm. tablets of chloroquine, or two 0·1 gm. tablets of paludrine, or two tablets of 0·3 gm. sodium bicarbonate once a week. The administration was continued for 40 weeks.

Among 125 persons receiving chloroquine, 2 developed overt malaria : of 104 receiving paludrine, 17 developed overt malaria : of 106 receiving sodium bicarbonate, 54 developed overt malaria. Chloroquine appeared to be responsible for nausea and vomiting in two patients, vertigo in one, and flatulence in one patient.

With the doses used chloroquine was a more efficient suppressive agent than was paludrine. *Norman White*

WALLACE, R. B. **Insecticides and** *A. maculatus*. *Med. J. Malaya*. 1948, Sept., v. 3, No. 1, 5–33, 1 plan & 8 charts.

On a rubber estate in Malaya of over 10,000 acres in typical *Anopheles maculatus* country, pre-war methods of control of hyperendemic malaria by anti-larval measures had proved unsuccessful and were replaced by a reliance on drug prophylaxis with atebrin [mepacrine] ; post-war atebrin was in turn replaced by paludrine. The mosquito nuisance, however, remains and demands alleviation. If residual insecticides could be proved to be effective it was hoped that the mosquito population would be reduced to the extent of preventing the annual epidemic of malaria and, indeed, that, in combination with the power of paludrine to prevent the fertilized female gametocyte developing to the sporozoite stage in the mosquito, a diminution in general incidence of malaria would occur.

Incessant biting of employees by bed-bugs and mosquitoes led to a trial of eight insecticides, four of which contained DDT, two Gammexane and two " Technical Chlordane."

Preliminary trials with 5 per cent. DDT in kerosene and with Gammexane dust in 1947 during the sixteen-week *A. maculatus* season gave " the impression that *A. maculatus* adults were completely eliminated from the lines", yet there was " no apparent effect on the breeding places nor on the malaria rate."

In the 1948 season, tests were conducted on the eight insecticides and the following entomological methods were used to assess the effects :—

(*a*) Weekly morning (5 a.m. till dawn) catches in dwellings.

(*b*) In one room only night (8 p.m. till midnight) catches of mosquitoes (i) caught in the act of biting, and (ii) engorged and resting on the wall or dead on sheets on the floor.

(*c*) Catches in untreated cattle sheds at the same periods.

(*d*) Catches in untreated control rooms at the same periods.

(*e*) Observations on breeding places.

The insecticides were applied at fortnightly intervals [precise dosage is not stated] during the *A. maculatus* season. Under laboratory conditions all the insecticides were lethal to mosquitoes ; none prevented *A. maculatus* entering rooms and feeding ; all reduced the early morning catches in varying degree, some to nil, without any evidence of dead mosquitoes. An irritant effect is ascribed to the DDT group affecting both morning and evening catches. Larval density in breeding places and the malaria rate were not affected. The author concludes that " There is still no proof that it [DDT] is the most effective insecticide against *A. maculatus* " though presumably the best of this series.

[These observations are comparable with those of Muirhead THOMSON concerning the effect of DDT on *A. gambiae* in Africa this *Bulletin*, 1949, v. 46, 439 ; the entomological methods used by the latter had a higher degree of accuracy. The Gammexane preparation used in Malaya was not the recent water-dispersible powder P 530 (now P 520) tested in East Africa with favourable results.] *R. Ford Tredre*

Downs, W. G., Colorado Iris, R. & Gahan, J. B. **Residual Effectiveness of DDT in the Third Season after Application.** *Amer. J. Trop. Med.* 1948, Sept., v. 28, No. 5, 741–5.

The mud-brick houses in an area of Mexico where *Anopheles pseudopunctipennis* is prevalent were treated with DDT in 1945, the dose being 190 mgm. per sq. ft. (6·7 ounces per 1,000 sq. ft.). An identical collecting procedure was followed before and after treatment, with the following results :—

Date	No. of collections	Average mosquitoes per building	
		Treated buildings	Untreated buildings
1945			
Before treatment ...	3	12	9
After treatment ...	11	0·005	59
1946	4	0·75	18
1947	2	1·35	14·8

The presence of DDT two and a half years after application was shown by biological and chemical tests. *G. Macdonald*

Morrison, D. B. & Jeskey, H. A. **Alterations in some Constituents of the Monkey Erythrocyte infected with *Plasmodium knowlesi* as related to Pigment Formation.** *J. National Malaria Soc.* 1948, Dec., v. 7, No. 4, 259–64, 3 figs.

Assuming that the parasite pigment is derived quantitatively from the host erythrocyte haemoglobin and that the total erythrocyte haematin is constant, the authors calculated total erythrocyte concentration in given samples of blood (monkey and duck) by measuring the total haematin, and the average effective number of pigmented parasites (*P. knowlesi* and *P. lophurae*) by determining the parasite haematin. Alterations in parasitized cells of total N, total lipides and total solids were also determined in relation to the amount of parasite haematin present.

In *P. knowlesi* malaria in *Macaca mulatta* they found that 0·76 per cent. of haemoglobin was converted to parasite haematin when 1·0 per cent. of erythrocytes were parasitized with the "average pigmented form of parasite." This result compared favourably with that of Ball *et al.* [this *Bulletin*, 1949, v. 46, 117] who found in two monkeys infected with *P. knowlesi* that 40 per cent. total haematin existed as free haematin when there was 56 per cent. infection of erythrocytes, and 49 per cent. as free haematin when there was a 62 per cent. infection ; these figures correspond to 0·72 and 0·79 per cent. of haemoglobin being metabolized to parasite haematin in a 1·0 per cent. infection.

The authors conclude that 76 per cent. of host cell haemoglobin in *P. knowlesi* infections in *M. mulatta* is converted into parasite pigment by an average pigmented form of parasite. Total N and total solids of the erythrocyte are reduced but there is an increase in total lipide, these changes presumably being brought about by parasite metabolism. *B. G. Maegraith*

Henderson, F. G., Rose, C. L., Harris, P. N. & Chen, K. K. **γ-Dichroine, the Antimalarial Alkaloid of Ch'ang Shan.** *J. Pharm. & Exper. Therap.* 1949, Feb., v. 95, No. 2, 191–200, 5 figs. [28 refs.]

In the search for new antimalarials during the late war, attention was again focussed on Ch'ang Shan, the root of an indigenous evergreen shrub of S.W.

China, much prized for its antimalarial properties there. The botanical name of the plant is now generally accepted as *Dichroa febrifuga*. [For recent developments on the chemistry of the active principles present see this *Bulletin*, 1946, v. 43, 1012; 1947, v. 44, 699, 964; 1948, v. 45, 578 and above, p. 611.] Substances have been obtained from the plant more active than quinine in *P. lophurae* infection of ducks and in *P. gallinaceum* infection of chickens. In China, one alkaloid isolated was named γ-dichroine (believed to be a quinazoline derivative), a crystalline substance of m.p. 160°C. In the present investigation this substance has been tested for antimalarial and other properties, in ducks infected with *P. lophurae* and canaries infected with *P. relictum*, determination of the median suppressive dose (SD50), that which reduces parasitaemia to half, in the case of γ-dichroine and quinine, showed that the former was very much more active. The new substance surprisingly proved more toxic to mice when given orally than by the intravenous route, and in lethal doses damage was done mainly to the liver. In pigeons the alkaloid had an emetic action as sometimes seen in man. Blood pressure and respiration in anaesthetized dogs was unaffected and intestinal peristalsis was stimulated. In unanaesthetized animals there was diarrhoea. In certain doses intravenous administration caused hyperglycaemia in rabbits. The drug also exerted an antipyretic effect.

J. D. Fulton

i. Wingstrand, K. G. **On some Haematozoa of Swedish Birds with Remarks on the Schizogony of** *Leucocytozoon sakharoffi*. *Kungl. Svenska Vetenskapsakad. Handl.* Stockholm. 1947, v. 24, No. 5, 31 pp., 19 figs. [34 refs.]

ii. ——. **Further Studies on** *Leucocytozoon sakharoffi*. *Ibid.* No. 8, 17 pp. 12 figs. [11 refs.]

i. A description is given of six species of *Leucocytozoon* including a new unnamed one in a rook, and of two species of *Haemoproteus*, including a new one, *H. buteonis* in a buzzard. The endocrine glands of two young crows (*Corvus corone cornix*) showed the presence of the asexual forms of *Leucocytozoon*, *viz.* very striking megalo-schizonts. They were found in the anterior and posterior portions of the pituitary gland, in a testicle, and in the thyroid. The youngest schizonts appear to develop in endothelial cells of capillaries. The young schizont is composed of a few " cytomeres," 2–3μ in diameter, and each cytomere is surrounded by a vacuole. The nucleus of the host cell enlarges as does the cell itself; eventually the diameter of the nucleus is enlarged 40 times, the cell itself measuring 470μ. In these later stages, the cytomeres form a continuous layer around the nucleus; each is about 15μ in diameter and contains numerous merozoites visible as deeply staining granules 1μ in size. A zone of cytoplasm free from cytomeres surrounds the host cell nucleus. In adult birds this type of schizont was absent; a smaller kind in the hepatic parenchyma is described but whether the latter structures are truly parasitic even the author appears to doubt.

ii. Material additional to that described above was examined in the organs of two half-grown crow nestlings which had suffered from very violent attacks of the disease (about 10 infected lymphocytes to 100 erythrocytes). The course of development of the megalo-schizonts was observed in the spleen where they occurred in abundance. The host cell appears to be a macrophage. Development is described all in terms of the " cytomere." The cytomeres split up into " sub-cytomeres," bladder-like bodies with the granules concentrated on the surface. Eventually, all differentiation is lost and a continuous mass of merozoites is formed outside the host cell nucleus. The merozoites exhibit bipolar staining. The ripe schizont bursts and discharges a cloud of merozoites into

the adjacent blood vessels. The granules give a positive Feulgen reaction only in the final stages ; earlier, the usual Romanowsky or haematoxylin stains fail to show any chromatin. This substance, however, can be impregnated with silver by using the Bodian technique and then is visible throughout the cycle.

[These observations confirm HUFF's work (*J. Infect. Dis.*, 1942, v. 71, 18) on another species of *Leucocytozoon*. The megalo-schizonts of the Swedish parasites, however, appear to be five times the size of the American ones, reaching nearly half a millimetre in diameter. In size, therefore, they form a link between the schizonts of *L. simondi* and the 2 mm. merocysts of *Hepatocystes kochi* [this *Bulletin*, 1948, v. 45, 683]. In the latter, the host cell becomes similarly enormously enlarged but the nucleus undergoes repeated divisions instead of growing into a body 190μ in diameter. The final product is alike in all three parasites, *viz.* a compressed mass of innumerable bipolar-staining merozoites, which escape into the blood to form gametocytes.]

P. C. C. Garnham

HART, J. W. **Observations on Blood Parasites of Birds in South Carolina.** *J. Parasitology.* 1949, Feb., v. 35, No. 1, 79–82.

The birds of a district in South Carolina, U.S.A., were examined in winter and summer for the presence of parasites in the blood : 4·9 per cent. showed infections in the winter and 1·6 per cent. in the summer. The following parasites were found : *Plasmodium circumflexum, elongatum, hexamerium, oti* and *relictum* ; *Haemoproteus, Leucocytozoon, Trypanosoma* and *Toxoplasma*. The majority of the birds were English sparrows (*Passer domesticus*). Sporozoite rates in the local *Anopheles* have been high, although human malaria cases were uncommon ; the possibility of an avian origin had, therefore, to be considered, and these observations provide some evidence that such an origin may have existed.

P. C. C. Garnham

OESTERLIN, M. Sulfonamidverbindungen bei experimenteller Vogelmalaria. [**Sulphonamide Compounds in Experimental Bird Malaria.**] *Zent. f. Bakt.* I. Abt. Orig. 1941, Aug. 1, v. 147, No. 5, 339–42, 1 fig. [17 refs.]

BLACKWATER FEVER

WEISE, W. Ueber das Pseudo-Methämoglobin (Methaemalbumin) N. H. Fairley. [**Pseudo-Haemoglobin (Methaemalbumin) Fairley.**] Reprinted from *Deut. Tropenmed. Ztschr.* 1941, v. 45, No. 7, 218–24. [17 refs.]

FAIRLEY's demonstration of the rapid development of methaemalbumin on the addition of an alkaline solution of haematin to plasma and heating to 40°C. [this *Bulletin*, 1935, v. 32, 210 ; 1937, v. 34, 841], suggests to the author that methaemalbumin is really only haematin dissolved in serum and not the firm chemical compound of haematin and crystalbumin that Fairley claimed. The author considers the production of haemochromogen after the addition of concentrated ammonium sulphide in Fairley's blackwater fever cases as proof of this, since SCHUMM regarded this reaction as evidence of the presence of haematin. (Fairley, on the other hand, believes Schumm's reaction indicates the presence of the pigment methaemalbumin and not haematin.)

The argument in this paper covers much the same ground as Fairley's original communications. The author points out that Schumm's test easily

distinguishes haematin from methaemoglobin and that haematin (as indicated by the test) has been found in the blood serum in many pathological conditions, including severe malignant tertian malaria. He confirms HEILMEYER'S observation that the spectrum of haematin dissolved in serum differs from that of alkaline watery haematin solution because it is combined with serum protein. In his view this combination is a loose one similar to other physiological combinations of substances with protein, for example " haemolytic " bilirubin. Fairley's pigment need not therefore be regarded as a firm chemical compound, in spite of its behaviour in the ultra-centrifuge or under electrophoresis. The production of haemalbumin on the addition of sodium hydrosulphite to methaemalbumin, as reported by Fairley, he regards as requiring further proof.

He confirms Fairley's observations on the slow production of methaemalbumin in mixtures of the haemoglobin and serum of mammals other than the human being and the ape, and reports his findings in a small series of experiments in which human, dog, rabbit and horse haemoglobins are compared in this respect. After 48 hours' incubation at 37°C. the mixtures of haemoglobin and sera all produced methaemoglobin, small amounts in the human mixtures, much larger in the others. On the other hand, " haematin " (as estimated by Schumm's test) was produced only in the human and dog mixtures. He suggests that this is because only easily split haemoglobins (such as human and dog) will give rise to haematin in serum. Other more resistant haemoglobins produce methaemoglobin only.

[The physiological and pathological importance of Fairley's observations with regard to methaemalbumin seems to the reviewer to be unaffected by this communication.] *B. G. Maegraith*

KHO LIEN KENG. Gestoorde nierfunctie bij zwartwaterkoorts. [**Disturbed Kidney Function in Blackwater Fever.**] *Med. Maandblad.* Batavia. 1949, Feb. 1, v. 2, No. 2, 46–51. [29 refs.]

The English summary appended to the paper is as follows :—

" Three cases of blackwater fever with renal damage are reported. The first patient showed, during a week after disappearance of the clinical symptoms, an isosthenuria at a rather normal diuresis. The second patient died anuric.

" The third one produced symptoms of glomerulonephritis after a second attack of blackwater fever. Follow up a year later still showed renal insufficiency (blood-urea 1·078 g liter, specific gravity of urine 1,004)."

TRYPANOSOMIASIS

VANDERPLANK, F. L. **Studies of the Behaviour of the Tsetse-Fly,** *Glossina pallidipes*, **in the Field : Influence of Climatic Factors on Activity.** *J. Animal Ecology.* 1948, Nov., v. 17, No. 2, 245–60. [17 refs.]

The author wishes to investigate the relation between the activity of a tsetse fly, *Glossina pallidipes*, and certain climatic factors. His method, in broad terms, is to tie up an ox and catch the flies that come to it, recording them in fifteen-minute spells throughout the day. At the same intervals he measures temperature, humidity, light and so forth. Conditions for this type of experiment seem to have been good for there is some indication that the tsetse population did not vary greatly over a number of months. If, therefore, differences in the numbers of flies caught were established they were due to differences

in activity ; one might reasonably try to relate them to climatic factors. Had there been large differences also in the population this work would have been very difficult.

A point of considerable interest is that for several of the physical factors middle values are associated with greater activity of the fly than either high or low values. For instance, within the limits of the conditions prevailing where the work was done, the insect became more active the brighter the light, but only up to a certain point : at midday on bright days the light was too intense and reduced the activity of the flies. The same was true both of humidity (measured by saturation deficiency) and of temperature : in each case there was a critical value above which the activity decreased. For instance, for temperatures up to 29°C. there was a positive correlation between the dryness of the air and the activity of the insect. But from 30°C. upwards the correlation was reversed and became negative, so that at the higher temperatures the drier the air the less was the activity of *G. pallidipes*. Throughout the paper full use is made of statistical methods and measures of significance are given.

There is an interesting comparison between the catch of *G. pallidipes* at different hours of the day in the thicket and out on the open hard pan. In the thicket, perhaps because the temperature never gets very high, and the light at midday is not very bright, the insect is active all through the day, indeed equally active all through the day. But outside on the hard pan, there is a great reduction of activity at noon and soon after, except on days when much light is absorbed by dust in the atmosphere or by cloud. It is a matter of some interest that figures collected by other authors in Italian Somaliland and Zululand can on the whole be reconciled with this author's own figures from Tanganyika.

In this paper the author makes use of several modern conceptions about tsetse populations and advances our knowledge of his side of the subject considerably. One might perhaps say that not every point in the argument is equally well established : the reviewer believes that there is one serious statistical misprint which it is not possible for the reader to correct. *P. A. Buxton*

MORRIS, K. R. S. & MORRIS, M. G. **The Use of Traps against Tsetse in West Africa.** *Bull. Entom. Res.* 1949, Mar., v. 39, Pt. 4, 491–528, 5 text figs. & 8 figs. on 2 pls. [16 refs.]

The authors describe their work in the savannah country in the north of the Gold Coast where *Glossina palpalis* and *G. tachinoides* are common along riversides. They have not only attempted control by trapping but they have tried to understand the underlying principles. The result is that the paper tells one something about the fly's view of the world and advances our knowledge of the subject considerably. The problem is practical, but the authors have not limited themselves solely to practical considerations.

Morris and Morris have tested a number of recognized types of tsetse traps and have developed one which they describe as the Animal Trap. It resembles a Harris trap but is much smaller, indeed about the size of a goat. [One notes incidentally that it is implied that sheep and goats are commonly fed upon by these insects, which we think is not the experience in some other parts of Africa.] Under their conditions the animal trap is the most efficient, among several types tested. In addition to comparing the efficacy of different types of trap, the authors have devoted much attention to comparing their Animal traps with teams of fly boys working in the same areas : no straightforward comparison is possible, the attractiveness of the trap and perhaps of the fly boys varying with season. They find, as others have, that the exact position

in which one places the trap is very important : it should be sited in an open feeding ground frequented either by man or animals. If it is placed close to an actual tethered animal, it catches more flies than if it is not.

Much of the authors' work has been done in small " sacred groves " where clearing is not possible for religious reasons. In these groves they have used traps at a density as high as twenty to the acre, but they still find that eradication of tsetse by trapping is not possible. Traps may, however, prove valuable to protect man from fly or sleeping sickness because they will catch a large proportion of the flies, perhaps quite quickly. Moreover the catch is highest in the dry season, when the contact between man and fly is likely to be closest because there are very few water holes and those generally in fly belts.

P. A. Buxton

Ferreira, T. Os trabalhos de combate à Glossina "morsitans", West. no Mutuáli. Relatório anual. [**Annual Report of the Campaign against** *Glossina morsitans* **in the Mutuáli Region.**] 68 pp., 5 charts, 4 diagrams & 4 maps. Colónia de Moçambique. Missão de combate às tripanossomíases. I.ª Subsecção de Entomologia. 1948. Lourenço Marques : Imprensa Nacional de Moçambique.

Scheff, G. J. & Thatcher, J. S. **The Role of Potassium as Cause of Death in Experimental Trypanosomiasis.** *J. Parasitology.* 1949, Feb., v. 35, No. 1, 35–40. [38 refs.]

" The survival time after trypanosome infection was found to be the same in the potassium tolerant and non-tolerant animals, suggesting that the potassium is not the causative agent of death, as recently advocated."

Labandera-Goñi, H. A proposito del primer caso de enfermedad de chagas comprobado en Florida. [**The First Proved Case of Chagas's Disease in Florida (Uruguay).**] *Arch. Uruguayos de Med., Cirug. y Especialidades.* 1948, Sept.–Oct., v. 33, Nos. 3/4, 119–22.

The English summary appended to the paper is as follows :—

" A description of the first proven case of Chagas Disease (benign acute edematous unilateral bipalpebral form) in a child, male in sex, domiciled in the Department of Florida [Uruguay] is presented."

Wood, S. F. **Additional Observations on** *Trypanosoma cruzi* **Chagas, from Arizona in Insects, Rodents, and Experimentally Infected Animals.** *Amer. J. Trop. Med.* 1949, Jan., v. 29, No. 1, 43–55, 1 map & 12 figs. on pl. [13 refs.]

This paper reports the results of surveys carried out in Arizona to determine the members of the sub-family *Triatominae* which are naturally infected with *Trypanosoma cruzi*. Incidentally, the first naturally-occurring infections in mammals—substantiated by xenodiagnosis—are also recorded.

The following species of reduviids occurring in the area have been found naturally infected with *T. cruzi*, the two first listed being here recorded as infected for the first time :—

Triatoma protracta,
Triatoma protracta woodi,
Triatoma rubida uhleri,
Triatoma longipes.

Thirty-nine wild-caught mammals were examined for the presence of trypanosomes in the blood by the fresh film method or in stained slides. Three were found to harbour a "*lewisi*" type of trypanosome.

Of the mammals mentioned, sixteen were examined in the laboratory by xenodiagnosis. Four animals proved to be infected but no trypanosomes were found in the blood nor did the tissues at post mortem reveal any parasites. [One presumes that the insects used were clean laboratory-bred individuals, but it is not stated.]

An account is given of various laboratory animals infected experimentally by the various strains of *T. cruzi* coming from reduviid bugs from various localities in the area under survey.

The results obtained included the demonstration of " leishmania " bodies in muscular tissue.

The usefulness of xenodiagnosis in the detection of naturally-occurring infections is emphasized. *H. E. Shortt*

PELLEGRINO, J. & BORROTCHIN, M. Inquérito sôbre doença de Chagas no Hospital da Santa Casa de Misericórdia de Belo Horizonte (Minas Gerais, Brasil). [**Cases of Chagas's Disease among Patients in a Hospital in Minas Gerais, Brazil.**] *Brasil-Medico*. 1948, Sept. 4–11, v. 62, Nos. 36/37, 314–15. English summary.

This short article appears to be a part of a fuller work which, when complete, is to form one of the publications issuing from the Oswaldo Cruz Institute. It is a summary of results obtained from examining 181 unselected patients at the Santa Casa de Misericordia Hospital in Belo Horizonte. The examination was thorough and included general physical examination, electrocardiograms, complement fixation with *T. cruzi* culture antigen, and any suspicious patient was further subjected to xenodiagnostic and X-ray tests.

Thirty-seven presented indications of infection with *T. cruzi* ; of 49 with cardiac disturbance 18 were due to Chagas's disease ; syphilis accounted for six. Of these 18, the majority showed changes in the right bundle of His and of QRS auriculo-ventricular blocks. Just half of those with chronic heart disease due to *T. cruzi* were under 30 years of age, whereas four-fifths of those with heart lesions of other origin were over that age. On the whole the complement fixation test was a valuable method of diagnosis (in 31 out of 37 cases), but only eight of the 31 gave a positive result to xenodiagnostic tests.

The chief vectors in Minas Gerais were *Panstrongylus megistus*, *Triatoma infestans* and *T. sordida* ; 12 other species of Triatomidae are found in the State, but they are not active vectors. Triatomidae were found in 204 of the 316 municipalities of the State and infected specimens were found in 143 municipalities. A chart has been drawn up showing the areas most highly infected. *H. Harold Scott*

DIAS, E., LARANJA, F. S. & PELLEGRINO, J. Estudos sôbre a importância social da doença de chagas. I. Inquérito clínico-epidemiológico feito nas vizinhanças de Bambui, Oeste de Minas. [**Studies of the Social Importance of Chagas's Disease. I. Investigation carried out in the Environs of Bambui, Western Minas Gerais.**] *Brasil-Medico*. 1948, Dec. 4, 11, 18 & 25, v. 62, Nos. 49, 50, 51 & 52, 412–13. English summary.

The evidence afforded by this investigation demonstrates very clearly the large part which infection with *T. cruzi* plays in producing cardiac disease, in this district at all events. [Studies in other districts will show whether this applies in them also.]

The authors examined persons engaged on the railway, including members of their families, altogether 312 individuals. One hundred and twenty-two

of these gave a positive complement fixation, 190 did not. In 62 the xeno-diagnostic test was carried out [whether from the positive, or negative, or both is not stated] and in five the result was positive. In all those studied similar tests were made—histories, symptoms, physical signs and electrocardiographic findings. The last is the most important from the point of view of this investigation. Among 104 of the 122 giving a positive complement fixation, 34 showed electrocardiographic changes (32·5 per cent.) ; among 176 negative to complement fixation six only showed changes (3·5 per cent.). The commonest of these disturbances was premature ventricular contractions and close behind came right bundle branch block and atypical QRS or T wave abnormalities ; other lesions observed were prolonged P-R interval and a certain degree of, even up to complete, A-V block.

Other causes of chronic cardiac disease were looked for and in 29 of the 34 patients no other cause could be found ; the remaining five had syphilis also, which might account for aortic disease and arteriosclerotic changes. Four of the former died within a year of the observations being made.

H. Harold Scott

LEISHMANIASIS

KIRK, R. **The Differentiation and Nomenclature of Leishmania.** *Parasitology.* 1949, Feb., v. 39, Nos. 3/4, 263–73. [119 refs.]

This paper is itself a review and therefore should be read in the original as it is not possible to condense the contents except in the most general way, which has been attempted here.

An account is given of the early history of the discovery of parasites of the genus *Leishmania*. This is followed by sections dealing with the differentiation of " species " of the genus, based on various grounds, morphological, clinical, serological and otherwise, which are shortly considered below.

Differentiation based on morphology.

The comparison of various strains of *Leishmania*, both cultural and in the Leishman-Donovan-body form, have led some workers to consider that differentiation is possible on grounds of size between *L. donovani* and *L. tropica*, while others have distinguished these species by the type of growth in Nöller's medium. Still other workers, however, have failed to confirm these distinctions.

Differentiation on clinical and epidemiological grounds.

These have been the main grounds on which leishmanial species have been separated, even though they are unsatisfactory from the systematist's point of view. After creation of the genus *Leishmania* for the parasite of Indian kala azar, other species were differentiated as similar parasites were discovered to be the aetiological agents in other clinical conditions such as dermal ulcers occurring in the Old and New Worlds (*L. tropica* and *L. brasiliensis*). Further creations were *L. infantum*, *L. nilotica*. *L. peruviana* and others.

Differentiation by results of animal inoculation.

The results obtained in this way have been contradictory and inconclusive. *Leishmania donovani*, the parasite of kala azar, may give rise to cutaneous lesions in experimental animals, while *L. tropica*, the parasite of oriental sore, may produce generalized infections. In these cases, again, no uniform results are obtained and the results of infection vary greatly in different strains of the same " species". Similar attempts to differentiate *L. chagasi* of South America from *L. donovani* by animal inoculations fail to pass the test of adequate experimentation.

Cross immunity tests

Without going into details of the results of cross immunity experiments cited, it may be said that here also there is a lack of agreement in the results obtained by various workers. Thus, some writers maintain that a previous infection with *L. donovani* confers immunity against *L. tropica*, but others have been unable to confirm this.

Serological Tests.

These have comprised attempts to produce specific agglutinating sera, complement fixation tests, the Rieckenberg (adhesion) phenomenon and other techniques. Results by different workers have been contradictory and inconclusive in so far as the differentiation of "species" by these means is concerned and the impression gained by experienced workers is that the clear-cut results originally claimed when a few strains only were studied experimentally become obscured when a larger number of strains is studied.

Xeno-differentiation.

This term has been coined to indicate the different behaviour of strains of *Leishmania* in different species of *Phlebotomus*. In a species of *Phlebotomus* which is the vector of a strain of *Leishmania*, the parasites develop in the anterior station but, at best, there is not at present sufficient accurate information to make this an easy or definite means of separating strains.

The implications of the various studies mentioned above are discussed in relation to the morphological basis of zoological nomenclature and it is pointed out that the taxonomic status of biological races has not been defined by systematists. In spite of this it is considered justifiable to recognize three species of *Leishmania*, *viz. L. tropica*, *L. donovani* and *L. brasiliensis* on account of the clinical differences exhibited in the infections caused by these parasites which have been under close observation for 50 years and have not changed their characters in spite of the innumerable parasitic generations which such a lapse of time implies. It is felt that such consistent behaviour implies corresponding biological differences in the parasites, which are hereditary and stable. The last section of the paper deals with the synonymy of the species of *Leishmania* occurring in man. *H. E. Shortt*

RAGHVAN, P. **Kala-azar : Report of a Case of Local Origin.** *Indian Physician.* 1949, Jan., v. 8, No. 1, 3–5.

Another case from Bombay [see this *Bulletin*, 1948, v. 45, 317].

ATHIAS, Mlle., TIMSIT, R. & ZERMATI. Un nouveau cas de kala-azar traité par le 2168 RP. [**A New Case of Kala Azar treated by 2168 RP.**] *Algérie Méd.* 1947, Apr., No. 4, 346–9.

PUELLO GARCIA, M. J. Leishmaniasis. [**History of Leishmaniasis in Colombia.**] *Rev. Facul. de Med.* Bogota, 1949, Jan., v. 17, No. 7, 338–59.

The first part of this article gives a sketch of the history of muco-cutaneous leishmaniasis, locally known as Puercas or Marranas [literally pigs or sows, but applied as an adjective to anything foul or dirty] in Colombia, from the first published description of a case in a boy, 11 years old, in July 1872. In the early days it was regarded as either syphilitic or a suppurating leprous lesion, and only at the end of the century were the differences noted between cutaneous leishmaniasis and cancer, scrofula, syphilis and other diseases. It was not until 1944 that a case was recorded by Dr. A. Gast Galvis as "The first case of visceral leishmaniasis in Colombia."

The author next notes the Colombian endemic foci of the disease and mentions nearly a score of them and then lists the possible transmitter ; there

are 7 species of *Phlebotomus* in Colombia, namely *P. squamiventris, evansi, panamensis, monticolus* var. *incarum, colombianus, osornoi* and *longipalpis*. The dog is probably the reservoir host and inoculation of dogs with human material produces lesions identical with the human disease and the sera of dogs with visceral localization give the same results as human sera. But the question of the dog being definitely the reservoir host is not yet proved, though no other animal seems to be likely.

For treatment the author uses diphosphate of chloroquinoline [chloroquine]. In solution this is stable at *p*H 4–6·5 and withstands a temperature of 121°C. for 40 minutes ; above *p*H 6·5 it decomposes. It is a white crystalline powder, with acrid, bitter taste. After experimental tests on rats, rabbits, dogs and monkeys the author tried the drug in human patients in the following doses *per os*. For very serious cases with extensive lesions, multiple and with perforation of the nasal septum ; first day, 1 gm. at 8 a.m., 0·5 gm. at 3 p.m. ; second day, 0·5 gm. at 8 a.m. and 3 p.m. ; third day, 0·5 gm. at 8 a.m. and 0·25 gm. at 3 p.m., altogether 3·25 gm. In cases of less severity, the dosage for the first day is the same, but on the two following days 0·5 gm. at 8 a.m. only, a total of 2·5 gm.

Twenty-one patients have had this treatment ; 10 are completely cured and their lesions cicatrized ; 3 are much improved with diminution of the lesions, less secretion, less itching and local pain, 3 others had improved markedly when they left and could not be followed up ; 3 more are at present under treatment and " show appreciable improvement " ; 2 have not responded to the treatment.

The author concludes that the results of this new treatment by oral administration of diphosphate of chloroquine are better than those from any of the drugs hitherto used ; the toxicity is low in contrast with the antimonials ; it is given *per os* and patients can be up and about and the cost is less than that of drugs previously used. [The doses of chloroquine appear to be high, compared with standard doses, used in the treatment of malaria.]

H. Harold Scott

FEVERS OF THE TYPHUS GROUP

Weyer, F. Vergleichende Untersuchungen an Rickettsien. [**Investigations into the Relationships of the Rickettsiae.**] Reprinted from *Ztschr. f. Naturforsch.* 1947, v. 2b, Nos. 9/10, 349–58. [14 refs.]

For four years the author has been investigating the rickettsiae of the louse-typhus (*Läusefleckfieber*) and flea-typhus (*Flohfleckfieber*) groups. Details of the studies, including the technical methods employed, are given in other recent papers [see also this *Bulletin*, 1949, v. 46, 537 and below].

The present paper consists chiefly of a long discussion of the remarkable variations observed in the habit of growth and virulence of *Rickettsia prowazeki* and *R. mooseri*, both of which in laboratory conditions have often been observed to become extracellular and at the same time non-virulent for lice and mice. The modified types may even be indistinguishable from the rickettsiae which are naturally extracellular and non-virulent for mice, *viz.*, *R. wolhynica*, *R. pediculi*, and *R. weigli*.

In several cases the modified types have reverted to the original type and have again become intracellular and virulent, though it has not been found possible to devise a method by which the reversal can be produced with uniform success.

Among the conditions in which changes in type have occurred are :—(1) the maintenance of strains by the customary laboratory methods, (2) intracoelomic inoculation of ticks, (3) transmission through ticks, fleas, and weevil larvae, and (4) storage for long periods of dried infected faeces of arthropods.

The author states that both *R. prowazeki* and *R. mooseri* may be so variable in laboratory conditions that the differences observed among individual strains of either organism can be greater than the differences usually relied on to distinguish between the two species of rickettsiae.

It is regarded as an open question whether the changes are due to inherent mutability of the organisms or to the simultaneous occurrence of intracellular and extracellular types, one or other of which predominates when environmental conditions become favourable for its development.

[The possible bearing of the mutability of the rickettsiae on changes in virulence of typhus infection during epidemics and on the carry-over of infection between epidemics is regarded as a subject for speculation.

Complement-fixation and mouse-protection tests might throw light on the question whether important qualitative changes have occurred in the antigenic and immunological properties of the modified strains of rickettsiae. Most of the changes in type seem to have occurred in very artificial conditions ; this factor must be taken into account when attempting to assess the bearing of the findings on the problems of human typhus.] *John W. D. Megaw*

WEYER, F. Die künstliche Infektion von Zecken mit Rickettsien und anderen Krankheitserregern. [**Artificial Inoculation of Ticks with Rickettsiae and other Disease Agents.**] *Zent. f. Bakt.* I. Abt. Orig. 1948, v. 152, 449–57.

Various ticks, especially *Ornithodorus moubata*, were successfully inoculated by the intracoelomic route with suspensions containing *Rickettsia mooseri*, *R. prowazeki*, and *R. wolhynica*. The agent of " atypical broncho-pneumonia " or " benign bronchopneumonia " (Herzberg) was also cultivated in the same way. [Apparently this was *R. burneti* see this *Bulletin*, 1949, v. 46, 541.]

Attempts were made, without success, to cultivate the viruses of mouse bronchopneumonia and influenza. In the abstract in English the influenza virus is wrongly referred to as the " Influenza bacillus."

Technical details are given of a large number of these experiments.

Only one out of three attempts to cultivate *R. wolhynica* was successful ; in this case tick suspensions made 69 days after inoculation were infective to lice by the intrarectal route.

Four out of five strains of *R. prowazeki* were cultivated in ticks, suspensions of which were found infective to mice and lice in tests made at intervals ranging from 14 to 262 days after inoculation. Two of the strains became extracellular and non-pathogenic for mice after passage through the tick, but one of these resumed the intracellular habit of growth and virulence for mice after three passages through lice, the other remained extracellular and non-pathogenic to mice after isolation from the eggs of the inoculated tick and later passage through lice.

In 15 sets of experiments with *R. mooseri* 13 positive results were obtained. In some cases intracellular strains were used and several of these became extracellular and non-virulent for mice ; in other cases extracellular strains became intracellular and regained their virulence *John W. D. Megaw*

Giroud, P. & Ciaccio, G. Inoculation de *Rickettsia prowazeki* et *mooseri* chez les poissons. Contrôle sérologique et immunité provoquée. [**Inoculation of Fish with *Rickettsia prowazeki* and *R. mooseri*. Serological Results.**] *C. R. Soc. Biol.* 1948, Dec., v. 142, Nos. 23/24, 1478–9.

The following is a translation of the authors' summary :—

Different fish may be infected with rickettsiae of epidemic typhus and react with the formation of agglutinins. The murine strain seems to be more adaptable than the epidemic. At least two passages can be maintained with the two strains, through the gills or other organs. The use of the liver or peritoneal organs, however, seems to be preferable.

[See also this *Bulletin*, 1949, v. 46, 451.] *H. J. O'D. Burke-Gaffney*

Mittermaier, R. Die Erkrankungen des Ohres beim Fleckfieber. [**Diseases of the Ears in Typhus Fever.**] *Deut. med. Woch.* 1948, Mar. 12, v. 73, Nos. 9/12, 109–11.

The author discusses in general terms the various complications of typhus fever that are associated with the organs of hearing. He believes that if all the minor degrees of deafness are included 80 per cent. of the patients may suffer from auditory troubles. He deals specially with septic infections of the middle ear, which usually appear about the 16th to the 18th day. He estimates that as many as 15 per cent. of patients with severe attacks may be affected, and he stresses the need for close observation of the patients with a view to early treatment of a complication which may have disastrous results.

John W. D. Megaw

Pfeffer, K. H. Über Störungen der vegetativen Regulationen in der Fleckfieberrekonvaleszenz. [**Disturbances of the Sympathetic Regulating Mechanism in Typhus Convalescents.**] *Deut. med. Woch.* 1948, Dec. 3, v. 73, Nos. 45/46, 596–8, 3 charts.

Good, N. E. & Kotcher, E. **Murine Typhus Fever in Louisville, Kentucky** *Pub. Health Rep.* Wash. 1949, Feb. 25, v. 64, No. 8, 229–37, 1 map.

In the present study, sera of 793 inhabitants of Louisville, Kentucky, yielded only three complement-fixation reactions against murine antigen at a titre of 1–4. Sera of 351 rats yielded only one positive reaction at a titre of 1–8.

In 27 per cent. of the rats caught in the market and business areas of the city *X. cheopis* were found.

The findings did not tend to justify the suspicion that murine typhus had extended to a significant degree as far north as Louisville.

John W. D. Megaw

Akle Delgadillo, J. & Pérez Rebelo, R. Existencia de tifo murino en Cd. Camargo, Chihuahua, Rep. Mex. [**The Presence of Murine Typhus in Camargo, Chihuahua.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1948, Sept., v. 9, No. 3, 195–7.

The English summary appended to the paper is as follows :—

"1. 350 Weil-Felix's tests were performed with human sera from Ciudad Camargo, Chihuahua, two of which were positives.

"2. These two positives sera fixed the complement with antigen of murine, and not with that of classic typhus.

"3. These results prove, first time, the presence of murine typhus in Ciudad Camargo, Chihuahua, Mex."

SMADEL, J. E., JACKSON, Elizabeth B., LEY, H. L., Jr. & LEWTHWAITE, R. **Comparison of Synthetic and Fermentation Chloramphenicol (Chloromycetin) in Rickettsial and Viral Infections.** *Proc. Soc. Exper. Biol. & Med.* 1949, Feb., v. 70, No. 2, 191–4, 2 figs. [11 refs.]

Chloromycetin, formerly prepared only from the mould *Streptomyces venezuelae*, has recently been produced synthetically and has been found to have the same physical and antibacterial properties as the fermentation product. The synthetic drug has now been found by the authors to be as effective as the original type in prolonging the life of embryo chicks infected with *Rickettsia rickettsi*, *R. akari*, *R. mooseri*, *R. prowazeki*, *R. tsutsugamushi*, psittacosis virus and a strain of lymphogranuloma virus.

In two batches, each of 8 mice, the synthetic drug was almost equally effective in preventing death after inoculation with about 40 lethal doses of *R. tsutsugamushi*.

In two cases of scrub typhus the synthetic drug produced the same dramatic improvement in the patients' condition as had been observed in other cases treated by the fermentation product. *John W. D. Megaw*

SMADEL, J. E. **Evaluation of New Drugs in the Treatment of Rickettsial Diseases.** *Bol. Oficina Sanitaria Panamericana.* 1949, Jan., v. 28, No. 1, 1–19, 11 figs. [19 refs.]

This is a succinct review of recent work on para-aminobenzoic acid and chloromycetin, the latter of which is now recognized as being remarkably effective in the treatment of the fevers of the typhus group transmitted by lice, fleas, ticks, and mites. *John W. D. Megaw*

BENINSON, J. & ANIGSTEIN, L. **Some Observations on the Effect of Cyto-chrome C in Rickettsial Infections.** *Texas Reports on Biol. & Med.* 1948, v. 6, No. 4, 486–92. [14 refs.]

"1. The apparent lengthening of the incubation period of Rocky Mountain spotted fever in guinea pigs following intraperitoneal injections of cytochrome C of varying concentrations as indicated has been postulated as being a nonspecific physiologic effect or a protein effect or both.

"2. Cytochrome C therapy begun on the day of fever in typhus and Rocky Mountain spotted fever in relatively large doses for two consecutive days did not alter the course of the fever."

HUEBNER, R. J., JELLISON, W. L. & BECK, M. D. **Q Fever—a Review of Current Knowledge.** *Ann. Intern. Med.* 1949, Mar., v. 30, No. 3, 495–509. [60 refs.]

NAUCK, E. G. & WEYER, F. Laboratoriumsinfektionen bei Q-Fieber. [**Laboratory Infection with Q Fever.**] *Deut. med. Woch.* 1949, Feb. 18, v. 74, No. 7, 198–202, 2 figs. [12 refs.]

In the course of the investigation previously described [this *Bulletin*, 1949, v. 46, 541] a laboratory outbreak of Q fever occurred at the Hamburg Tropical Diseases Institute. During a period of three months, beginning November 21, 1947, seven confirmed and four probable cases occurred, and in a footnote mention is made of two further confirmed cases.

The outbreak, which is described at length, appears to have been very like the laboratory outbreaks already reported from the U.S.A. and Australia. Rickettsiae were isolated and detected microscopically in stained smears made from animals and arthropods inoculated with the blood of four patients.

The methods of diagnosis included (1) intraperitoneal inoculation of mice with sputum of patients, (2) inoculation of mice with blood, (3) inoculation of guineapigs, followed by transfer through mice and ticks, (4) feeding of ticks, followed by transfer through mice, (5) feeding of lice followed by transfer through mice.

Complement-fixation tests could not be carried out because enough antigen was not available, but there seems to be no doubt regarding the nature of the disease.

The most likely mode of infection was thought to have been inhalation of infected dust. *John W. D. Megaw*

Combiesco, D. & Dumitresco, N. Survie *in vitro* de *Rickettsia burneti* de la fièvre Q en Roumanie. [**Survival** *in vitro* **of** *Rickettsia burneti* **in Rumania.**] *Ann. Inst Pasteur.* 1949, Jan., v. 76, No. 1, 79–80.

A number of blood samples were collected from guineapigs infected with *Rickettsia burneti* isolated in Rumania, and after clotting were covered with a layer of a mixture of oil and vaseline. The samples were kept at room temperature and tested at intervals by guineapig inoculation. Typical febrile reactions were caused in animals tested up to eight months, and a mild reaction occurred in an animal tested nearly 300 days after the preparation of the sample. After 11 months the blood became laked though it was still free from bacterial contamination ; it produced no definite reaction in the guineapig that was tested.
John W. D. Megaw

Combiesco, D., Combiesco, Cornelia, Dumitresco, N., Popesco, C. & Zarnea, G. Diagnostic rétrospectif par la réaction de fixation du complément d'un foyer roumain de fièvre Q. [**Retrospective Diagnosis of Q Fever in Rumania by the Complement-Fixation Reaction.**] *Ann. Inst. Pasteur.* 1949, Jan., v. 76, No. 1, 81–2.

In March and April 1947, nine persons employed at the antirabic section of the Institute of Serology of Constanza, Rumania, were attacked by a fever which could not be diagnosed at the time. All the patients had been engaged two to three weeks before the onset, in one capacity or another, in shearing sheep which had come from the neighbouring area. Seven of the patients were attacked between March 28th and April 6th, the other two were attacked on April 11th and 23rd, respectively.

[The interest of the outbreak consists in its being the first to be recognized in Rumania, rather than in the retrospective diagnosis which was made by the complement-fixation test early in May, of the same year.]
John W. D. Megaw

Weyer, F. Ueber *Rickettsia wolhynica* und die Diagnose des Wolhynischen Fiebers durch den Läuseversuch. [*Rickettsia wolhynica* **and the Diagnosis of Trench Fever by the Louse Test.**] *Zent. f. Bakt.* I. Abt. Orig. 1948, v. 152, 403–14. [15 refs.]

In 47 out of 146 cases of trench fever *R. wolhynica* was isolated from batches of lice which had been allowed to feed on the patients. In a number of cases the diagnosis could not have been made with certainty on clinical grounds. Scanty yolk-sac cultures were obtained in some cases from suspensions of the infected lice and the cultures were sometimes infective for lice by intrarectal inoculation, but it was not found possible to maintain the organisms by serial yolk-sac cultures.

The louse suspensions were not infective to mice by intranasal or other routes. Transfer of the rickettsiae to headlice and ticks (*Ornithodorus moubata*) were made by methods already described by the author [above].

Dried faeces of infected lice were still infective by intrarectal inoculation for body-lice after storage for 2½ years. *John W. D. Megaw*

BARTONELLOSIS

Silva Peralta, P. Un caso de neuro-bartonelosis. Tratado por penicilina. [**A Case of *Bartonella* Infection with Nervous Symptoms.**] *Rev. Méd. Peruana.* 1948, Oct., v. 21, No. 238, 641–50.

The patient, a girl of 15 years, was taken ill with a general feeling of malaise and intense fronto-occipital headache, accompanied by tinnitus. Her temperature on the third day was 38°C. She also complained of acute epigastric pain with nausea, which, however, soon left her, to return again 3 weeks later and again disappear. On or about the 14th day of disease she had wandering pains in the bones and became progressively weaker so that after 4 days she could not leave her bed; the left leg felt cold and numb, vision became blurred, "people appeared like shadows," and she was very breathless. She lost "a considerable amount of weight".

Clinically, she was thin and pale; respirations 35 per minute, pulse 140. Muscles tender, especially those of the neck, lips tremulous. Deep reflexes were exaggerated [they are usually said to be diminished or even lost in the severe anaemia of Carrión's disease]. There was no change in sensation. A functional presystolic bruit was heard over the aorta, the pulmonary and the tricuspid areas, but not propagated; lungs normal. There was slight enlargement of the cervical, inguinal and femoral glands which, however, were painless and mobile. Blood examination: red cells 950,000 (next day 895,000), leucocytes 10,950 (11,350 next day) per cmm. and 60 per cent. of the red cells showed *Bartonella*; there were anisocytosis and poikilocytosis, and 16 per cent. were normoblasts.

Treatment with penicillin was started on the first day that the patient came under the author's observation, the 24th day of disease; she was given 30,000 units every three hours, intramuscularly. Four days later, when 600,000 units had been given, the red cells had increased to 1,380,000 and the white reduced to 7,950 and *Bartonella* were no longer seen in the blood. Improvement was uninterrupted and 10½ weeks after the treatment was started blood examination showed red corpuscles 4,400,000, leucocytes 7,950 per cmm. The reflexes became normal, vision improved in a fortnight and was normal in 3 weeks, and, helped by passive movements, the muscular weakness cleared up. Besides the penicillin, 5 million units in all, the patient received liver extract, vitamin C 500 mgm. and vitamin A 100 mgm. daily. *H. Harold Scott*

YELLOW FEVER

STEFANOPOULO, G. J. & DUVOLON, S. Réactions observées au cours de la vaccination contre la fièvre jaune par virus atténué de culture (souche 17 D). A propos de 20.000 vaccinations pratiquées par ce procédé à l'Institut Pasteur de Paris (1936–46). [**Reactions during Yellow Fever Vaccination with Attenuated 17 D Virus in 20,000 such Vaccinations in the Pasteur Institute Paris in 1936-46.**] *Bull. et Mém. Soc. Méd. Hôpit de Paris.* 1947, Nos. 32/33, 990–1000. [26 refs.]

In this review of 10 years' experience of inoculation with the yellow fever vaccine the authors draw particular attention to the lack of harmful reactions in the recipients of the chick embryo vaccine containing the attenuated strain 17D of yellow fever virus. The neurotropic mouse brain vaccine has produced some severe reactions affecting the nervous system particularly in some cases, but they observed no bad reaction in 2,470 infants aged 15 days to 10 years who received the 17D vaccine. The neurotropic mouse brain vaccine has also been known to cause severe reactions in persons past middle age but the authors have seen no severe reactions in 1,500 people aged 45 to 88 who received the 17D vaccine.

The authors have tended to refrain from giving other injections in the week preceding and week following the yellow fever vaccine inoculation.

They draw particular attention to the necessity to ensure beforehand that those to be injected are not sensitive to egg protein. *F. O. MacCallum*

DENGUE AND ALLIED FEVERS

SABIN, A. B. & YOUNG, I. **A Complement Fixation Test for Dengue.** *Proc. Soc. Exper. Biol. & Med.* 1948, Dec., v. 69, No. 3, 478–80.

The antigen used was extracted with benzene from the brains of 3–14-day-old mice inoculated intracerebrally with a Hawaii strain of dengue virus which had been greatly exalted in virulence by repeated passages through mice of three to four days old. With this antigen complement-fixation titres of 1–64 to 1–256 were observed within two to six weeks of inoculation, in human volunteers, rhesus monkeys, and chimpanzees, infected with the homologous strain of human virus. The reaction persisted for many months ; titres ranging from 1–4 to 1–16 were observed up to 52 months after infection. Human volunteers inoculated with immunologically distinct strains of human virus gave titres of 1–16 or less, and within six months the reactions became negative. These volunteers developed little or no neutralizing antibody for the Hawaii virus, neither did rhesus monkeys inoculated with the same strains though they gave complement-fixation titres as high as 1–512 : but even at the lowest titres the reactions were incomplete (2–3 plus) and they became negative 6–10 weeks after inoculation. On the other hand a rhesus monkey inoculated with the Hawaii strain developed neutralizing antibodies at high titres though the complement-fixing titre was only 1–16 against the homologous antigen.

Human volunteers inoculated with a live vaccine made from mouse-adapted Hawaii virus became immune to unmodified human virus though the complement-fixation test remained negative.

Sera of persons who had been attacked by dengue two years previously in Hawaii, Japan, Singapore, Java, and New Guinea, contained high-titre neutralizing antibodies against the Hawaii virus and also gave complement-fixation

titres of 1–16 to 1–64. Other persons, 11 months after attacks of dengue in Guam, had no significant neutralizing antibodies against the Hawaii virus, and their fixation titres were 1–2 to 1–8.

Volunteers infected with sandfly fever virus gave negative complement-fixation reactions against the Hawaii antigen. Rhesus monkeys infected with the French neurotropic yellow fever virus also gave negative reactions seven weeks after inoculation, but 8–10 days after large "booster" doses of the neurotropic or the Asibi viscerotropic yellow fever virus they gave positive reactions at titres of 1–4 to 1–32. This result was regarded as evidence of an antigenic, if not an immunological, relationship between the viruses of dengue and yellow fever.

[The picture is greatly confused by the occurrence of antigenetic and immunological differences in the strains of dengue virus.] *John W. D. Megaw*

PLAGUE

FRANCIS, E. **Twenty-Five Year Survival of a *Pasteurella pestis* Culture without Transfer.** *Pub. Health Rep.* Wash. 1949, Feb. 25, v. 64, No. 8, 238–40.

In 1923 a set of 48 slope cultures of virulent *Pasteurella pestis* was prepared on beef-infusion agar and stored at 5–10°C. In 1943 subcultures were made and 33 of these gave luxuriant growths. The original cultures found alive were again examined in 1948 and 25 were still alive; subcultures made from them caused febrile reactions in guineapigs after subcutaneous inoculation, and the three animals that died showed typical lesions of acute plague, including the presence of numerous bacilli in smears of the spleen and lymph glands. The sugar reactions were exactly the same as those observed in 1923 and intermediate tests.

The maintenance of a liberal supply of water of condensation was considered important: tightly fitting cork stoppers, which had just been dipped in a mixture of paraffin and vaseline, were used.

The surviving 25 cultures and a set of 40 subcultures made in 1924 are being stored for tests in future years. *John W. D. Megaw*

MEYER, K. F. & HOLDENRIED, R. **Rodents and Fleas in a Plague Epizootic in a Rural Area of California.** *Puerto Rico J. Pub. Health & Trop. Med.* 1949, Mar., v. 24, No. 3, 201–9. [Refs. in footnotes.] [Spanish version 210–20.]

The authors state that the observations made in this study conclusively prove for the first time that plague may be spread from wild to domestic rodents.

In April, 1946, rats were reported to be dying in unusual numbers on a ranch near Santa Paula in California. A thorough ecological investigation was promptly carried out in the area. The most significant observations were as follows: Plague infection was demonstrated in four out of 15 tissue pools made from 42 *Rattus rattus rattus* and in two out of three specimens of *R. norvegicus*. Only three ground squirrels were found surviving on the ranch, infection was found in two of these, and also in one cottontail rabbit.

Infection was found in three of 10 pools made from 147 fleas collected from 40 of the rats, in a pool of 28 fleas from house mice and in a pool of four fleas from a harvest mouse.

The flea *Xenopsylla cheopis* was completely absent. One-quarter of the fleas found on rats were the ground-squirrel fleas *Diamanus montanus* and

Hoplopsyllus anomalus; these were believed to have transmitted infection from ground squirrels to the rats and also from rat to rat, because the other fleas found on the rats were the relatively poor vector, the mouse flea (*Leptopsylla segnis*) and a few fleas of the species *Nosopsyllus fasciatus*.

No rat fleas were found on any of the 53 squirrels taken in the vicinity of the ranch so that transmission from rat to squirrel was regarded as having been unlikely to occur.

In view of the findings the authors stress the necessity for effective rat control in places where plague occurs among wild rodents.

The paper contains a great deal of documented information regarding the rodents and fleas known or suspected as agents in the transmission of epizootic plague in the U.S.A. *John W. D. Megaw*

CHOLERA

Gallut, J. Contribution à l'étude de l'antigène thermostable du vibrion cholérique. Applications pratiques de l'analyse antigénique *O*. [**Study of the Thermostable Antigen of the Cholera Vibrio and its Practical Applications.**] *Ann. Inst. Pasteur.* 1949, Feb , v. 76, No. 2, 122–35, 1 fig.

The author undertook an antigenic analysis of a series of vibrios, including those isolated during the epidemic in Egypt in 1947, on the lines followed by Burrows, Mather, McGann and Wagner [this *Bulletin*, 1947, v. 44, 422] who had distinguished a total of 13 different antigenic fractions in their collection of cholera and non-cholera vibrios. The group antigen of *V. cholerae* had been designated A and the major specific factors of the Ogawa and Inaba types B and C respectively. The additional 10 fractions were D to M.

Out of 82 strains examined by the present author 61 were classified as agglutinable and 21 as inagglutinable vibrios. The first group consisted of :—

35 Egyptian strains (1947)—34 Inaba, 1 atypical.

14 established laboratory cultures—4 Inaba, 8 Hikojima, 2 Ogawa.

12 El Tor strains—2 Inaba, 10 Hikojima.

The atypical Egyptian strain contained the A antigen only.

The second group of inagglutinable vibrios could not be classified and were considered to be non-cholera vibrios.

The strains, examined by means of monospecific or bispecific sera for the different fractions, prepared by absorption, gave the following results :—

Antigen	61 agglutinable strains %	21 inagglutinable strains %
A	100	0
B	32	47
C	95	14
D	45	19
E	47	9
F	26	0
G & J	1·6	19
H & M	3	4
I & K	18	9
L	47	28

The majority of the strains possessed 3 or 4 of the antigens.

As the A antigen was present in all the agglutinable strains examined and absent from all the inagglutinable strains the author concludes that the demonstration of its presence, regardless of the titre of agglutination, is necessary and sufficient for the diagnosis of *V. cholerae*, the El Tor vibrios, which do not show any difference in antigenic structure from the cholera vibrio, being differentiated by the usual haemolytic test. The demonstration of the B and C antigens will serve to distinguish the Ogawa, Inaba and Hikojima types, but only if present along with the A antigen as these fractions have been found in the " inagglutinable " vibrios. It is considered that the use of monospecific sera prepared for the B and C factors may lead to error in the diagnosis of the three types on account of the presence of antibodies against subsidiary fractions, unless the complete antigenic formulae of the strains used in manufacture have been ascertained.

In view of the presence of the B and C antigens in non-cholera vibrios it is concluded that these are non-specific. No importance is attributed to the D to M antigens from the point of view of diagnosis, although these may be of interest in relation to the geographical distribution of strains.

The selection of strains for cholera vaccine is discussed in the light of the findings. It is suggested that stock vaccine should contain all 13 antigenic fractions and that the vaccine should be modified during the course of an epidemic in accordance with the predominance of the several factors found in the strains isolated. In the absence of detailed information on the antigenic structure the alternative empirical measure might be the inclusion of a number of strains in the vaccine. At the Pasteur Institute of Paris six strains, possessing between them most of the fractions, are used for manufacture.

In his examination of the Egyptian epidemic strains the author found the predominant antigens to be A, C, D, E and L and he considers that the optimum vaccine under the circumstances would have been one that contained these 5 factors. As no Ogawa strains were isolated the point is raised whether the use of a vaccine containing equal proportions of Ogawa and Inaba strains may not have entailed the risk of the production of inappropriate antibodies and an insufficient level of those which would be useful. *J. Taylor*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

STEWART, I. S. **Dysentery in South Persia.** *Brit. Med. J.* 1949, Apr. 16, 662–3.

This survey concerns a permanent and static civilian population and therefore has a certain value greater than surveys of the same diseases under war conditions. The statistics are based upon the initial laboratory examination of stools from all cases regarded as dysentery in the Anglo-Iranian oil company's 30,000 male artisan employees on Abadan Island.

The rarity of amoebiasis is specially commented upon. Proved amoebic dysentery accounted for only 3·8 per cent., whereas proved bacillary infections accounted for 37·3 per cent., and a further 56·6 per cent. were of bacillary type, but unproved. Diagnostic findings are classified below :—

Amoebic dysentery in which vegetative *E. histolytica* was the sole agent found	52
Cases failing to respond to sulphaguanidine and in which *E. histolytica* was found later	2
Cases failing to respond to sulphaguanidine and treated as amoebic dysentery without proof	1
Balantidial dysentery	13
Pure bacillary infections :—	
Shigella flexneri	353
,, *schmitzi*	49
,, *sonnei*	97
,, *shigae*	19
,, *boyd*	22
Mixed dysentery :—	
E. histolytica and *Sh. flexneri*	3
,, and *Sh. boyd*	2
Balantidium coli and *Sh. flexneri*	2
,, ,, and *Sh. sonnei*	2
Bacillary type cases with negative culture responding to sulphaguanidine	698
Admitted late without laboratory investigation and responding to sulphaguanidine	115
TOTAL	1,430

In the search for carriers the following procedure was adopted. Each patient was detained in hospital after the cessation of sulphaguanidine therapy, the next stool was then cultured and the patient discharged without waiting for the result. Those found positive were readmitted and given a course of 100 gm. of the drug. All were then found to be free of infection.

The table of carriers is as follows :—

Organism	Carriers	Total Recorded	Percentage of Total
Sh. flexneri	21	358	5·9
,, *sonnei*	8	99	8·1
,, *schmitzi*	2	49	4·1
,, *shigae*	1	19	5·3
,, *boyd*	3	24	12·5
TOTALS	35	549	—

Amoebic dysentery was treated with sulphaguanidine (4 gm. every four hours to a total of 20 gm.), followed by 10 days of emetine (1 grain daily) and five days of quinoxyl (0·25 gm. three times daily by mouth and a retention enema of 5 gm. in 200 cc. of saline each evening). Seven patients relapsed within a year.

Bacillary dysentery was treated with sulphaguanidine (4 gm. every four hours night and day) until patients were afebrile and symptomless. The dosage for the different groups is analysed in a table and the average requirement for each group is given.

The only significant complication was acute hepatitis, which occurred in 10 cases. There were no deaths in the series. *P. Manson-Bahr*

ANASTOPOULOS, B. **A Preliminary Note on Routine Culture Methods for *Endamoeba histolytica*.** *Puerto Rico J. Pub. Health & Trop. Med.* 1949, Mar., v. 24, No. 3, 240–42. [Spanish version 243–5].

In Porto Rico, the author cultured 100 faecal samples, ½ to 24 hours old, for *Entamoeba histolytica*. The Boeck-Drbohlav medium was used [this *Bulletin*, 1925, v. 22, 727], with Locke solution, inactivated human serum and rice powder : omission of the serum did not appear to affect the results.

Subculture was made every 48 hours on 2 to 4 occasions each (in one case, subculture was continued for 5½ months).

All but one of the specimens which were positive microscopically for *E. histolytica* were positive in culture : 10 which were negative microscopically were positive in culture. Excystation usually occurred in the first culture, though in a few cases amoebae grew only after the first or second transplant.

A table shows the percentage positive findings of intestinal protozoa in the stool, by direct and by culture examination. In the case of *E. histolytica*, 7 per cent. were positive microscopically and 16 per cent. on cultivation.

Another table shows the incidence of protozoa among various groups of Porto Ricans, based on single stool examinations, as found by different workers [see this *Bulletin*, 1928, v. 25, 244 ; 1934, v. 31, 281 ; 1935, v. 32, 244 ; 1946, v. 43, 1143]. The present author's finding of 17 per cent. in the 100 samples studied " indicates a slightly higher incidence of the parasite than has been reported to date from Puerto Rico". [But this does not take account of YOUNG and FELSENFELD's finding of 17·33 per cent. of *E. histolytica* among patients in Porto Rico, by means of direct smear and flotation : see this *Bulletin*, 1948, v. 45, 1005.]

The author considers that this cultural method may be used for routine diagnosis of intestinal protozoa, especially where undifferentiated pre-cystic stages or a few doubtful cysts are found by other methods.

H. J. O'D. Burke-Gaffney

SHAFFER, J. G., RYDEN, F. W. & FRYE, W. W. **Studies on the Growth Requirements of *Endamoeba histolytica*. IV. Further Observations on the Cultivation of *E. histolytica* and other Intestinal Protozoa in a Clear Medium without Demonstrable Bacterial Multiplication. Some Modifications and Simplifications of the Medium.** *Amer. J. Hyg.* 1949, Mar., v. 49, No. 2, 127–33.

The medium previously described by these authors [this *Bulletin*, 1948, v. 45, 786, 787, 1001] has been simplified by the omission of the filtrate of the bacterial complex, and now consists of the following :—

2 cc. normal saline,
0·25 cc. normal horse serum,
500 Oxford units of penicillin G sodium,
2·5 cc. preconditioned thioglycollate medium.

The last ingredient is the supernatant fluid from a centrifuged 24-hour culture of the special streptobacillus. It contains trypticase, dextrose, salts, methylene blue, agar, sodium thioglycollate, and between 10,000 and 100,000 streptobacilli per cc. It is highly labile and must be used within a few minutes of preparation. Anaerobic conditions are essential for successful cultures. The first isolations must be into media containing larger quantities of antibiotics (1,000 Oxford units of penicillin and 1,500 units of streptomycin per cc.). The technique is unsuitable for routine diagnostic procedures, but its employment will help in determining the food requirements of intestinal protozoa.

Six strains of *E. histolytica* have been isolated and maintained in the new medium, including one strain derived from cysts alone. A culture of *Entamoeba*

coli is being maintained in the presence of a bacterial contaminant. *Trichomonas vaginalis* and *T. hominis* grow with great ease and can be isolated from old specimens with no visible organisms. *Balantidium coli* also grows easily, but streptomycin inhibits the establishment of the initial cultures. Attempts to cultivate *Endolimax nana* and *Giardia intestinalis* were unsuccessful.

P. C. C. Garnham

MILLER, M. J. & FIRLOTTE, W. R. **Studies on Amoebiasis in Canada. Part II. A Method for obtaining Viable Cysts of *Entamoeba histolytica* free from Bacteria.** *Canadian J. Res.* Sect. E. Med. Sci. 1948, Dec., v. 26, No. 6, 299–302, 3 figs. (2 on pl.)

Inoculation of a modified Boeck & Drbohlav medium with sterile cysts of *Entamoeba histolytica* was performed in the following manner. Infected stools were obtained from inhabitants of a boys' orphanage. Cysts were concentrated by a zinc sulphate flotation method and were washed and suspended in sterile Ringer's solution to which penicillin (500 units per cc.) and streptomycin (1000 units per cc.) had been added. A resistant streptococcus was eventually eliminated by picking up the cysts with a micro-pipette and resuspending them in Ringer's solution plus antibiotics, the process being repeated five times. Details of a modified micro-pipette apparatus are given. The entire procedure takes about 8 hours to complete.

The method was devised in order to test the growth requirements of the amoebae. Various strains of bacteria were added to the culture tubes in order to discover those which best sustain growth. It is stated that the details of these experiments will be communicated later [for Part I of this series, see this *Bulletin*, 1948, v. 45, 1083].

P. C. C. Garnham

LYON, E. **Chronic Hepatitis in connection with Amoebiasis.** *Acta Med. Orientalia.* 1948, Sept.–Oct., v. 7, Nos. 9/10, 175–81. [18 refs.]

Four cases of chronic amoebic hepatitis are described. The author considers that two aetiological factors must be taken into consideration—an organotropic factor owing to the affinity existing between the amoebiasis and the liver—and an allergic one which is mainly brought about by constitutional features.

The main symptoms are paroxysmal pain and swelling of the liver. The functional liver damage gradually subsides.

A prompt response to emetine and yatren treatment was not noted. No efforts should be spared to protect the liver tissue : a low fat, but high carbohydrate and protein diet is required. Owing to the patients lack of appetite casein hydrolysates had to be used in order to avoid protein exhaustion. In particularly violent attacks of pain, sympathetic anaesthesia (paravertebral block) may be indicated, but antistin orally has been given with good results.

P. Manson-Bahr

TURNER, E. A. **A Case of Cerebral Amoebic Abscess treated by Modern Chemotherapy.** *J. Neurol., Neurosurgery & Psychiatry.* 1948, Nov., v. 11 (n s.), No 4, 291–3.

STEIN and KAZAN in 1942 (*J. Neuropath. Exper. Neurol.*, 1942, v. 1, 32) described the sixtieth case of cerebral amoebic abscess in the literature ; in only fifteen of the sixty were amoebae actually seen in the contents of the abscesses.

It is a matter for speculation whether cerebral amoebic abscess may not be curable with modern chemotherapy.

In this paper, the evidence in favour of the amoebic origin of the multiple cerebral abscesses is open to criticism. The patient, a soldier, had served only nine weeks in India before his admission to a military hospital. He presented the classical signs of cerebral abscess in the temporal lobe. In the pus abstracted through a burr hole by left temporal incision chains of streptococci were seen in a direct smear. Later the brain was tapped again and a second intracerebral abscess was entered behind the first. The pus was at first thin and watery and on direct examination numerous vegetative amoebae, actively mobile were seen in a slide. Cultures later produced non-haemolytic penicillin-resistant streptococcus. At necropsy the brain showed widespread meningo-encephalitis with the left hemisphere riddled with abscesses. In sections groups of streptococci were seen but no amoebae.

The patient was treated with sulphonamides, penicillin, streptomycin and emetine, but the last-named was only begun 3 months after the illness started. The illness lasted for 4½ months and ended fatally. *P. Manson-Bahr*

ZUIDEMA, P. J. Over emetine-intoxicatie. [**Emetine Intoxication.**] *Med. Maandblad.* Batavia. 1949, Feb. 1, v. 2, No. 2, 33–7, 1 chart.

The English summary appended to the paper is as follows :—

" In an Indonesian patient, 52 years old, severe myocardial damage occurred after 9 subcutaneous injections of 60 m.g. emetine each, corresponding with 7 m.g. emetine per K.G. body weight. The pulse rate suddenly rose to 126. The electrocardiogram revealed a lowered ST segment in Lead 1 and 2, a negative T in Lead 2 and 3 and a flat T in Lead 1. No other signs of intoxication were noted.

" Notwithstanding absolute rest in bed it took 3 weeks for the pulse rate to drop gradually to its original height. Another electrocardiogram, taken 2 weeks after the first, showed that the abnormalities had disappeared for a great deal.

" Probably in this patient a high individual susceptibility existed for the drug. This is also suggested by the history of the patient since in 1918 after 7 injections of emetine (dosage not known) a complete paralysis of the extremities occurred, for which a stay of several weeks in hospital became necessary.

" At the present time cardiac damage was the only clinical evidence of intoxication. It is suspected that organic heart disease existed already before emetine treatment was initiated."

WESTPHAL, A. & MARSCHALL, F. Amöbenruhr bei Katzen auf bakterieller Grundlage. [**Amoebic Dysentery in Cats in relation to Associated Bacterial Infection.**] Reprinted from *Virchows Arch. f. Path. Anat. u. Physiol.* 1941, v. 308, No. 1, 22–44, 9 figs.

The connexion between the establishment of amoebic dysentery and previous bacterial injury has been established by WESTPHAL in man [this *Bulletin*, 1939, v. 36, 288] and DESCHIENS [*ibid.*, 290] and others in cats ; and this work suggests a combined action. The present work has been planned on a different basis in that the bacteria used had been associated with a strain of *E. histolytica* which had been rendered virulent for cats. By comparison of infections with bacteria alone with those caused by the combined amoebic action it was hoped to decide, by means of rectal injections, what particular rôle the amoebae played. From experiments conducted on these lines it was decided that the symbiotic bacteria alone sufficed to bring about fatal dysentery in the majority

of cases. The clinical course of the disease in cats with pure bacterial infections and those which were also infected with amoebae ran a parallel course. The majority of animals died after a week and a few after two days. They wasted away with fever and passed diarrhoeal blood-stained stools.

Histopathological studies revealed extensive mucosal necrosis in the bacterial infections, with oedema and hyperaemia of the submucosa. The bowel lumen was filled with detritus and mucus and the inflammatory process extended into the small bowel. In some cases the lungs, liver and spleen were affected.

In the majority in which combined infection with amoebae had been established the cellular picture was identical, save that in the most extensive necrotic areas amoebae could be demonstrated. It is not suggested that these cases in which the amoebae lived in the necrotic detritus could be regarded as genuine cases of amoebic dysentery. In genuine intestinal amoebiasis the amoebae burrow into functionally healthy tissues in contrast to the former condition where these organisms are merely existing in the form of exaggerated intestinal parasitism [as opposed to tissue parasitism]. Quite exceptionally the combined amoebic infection loses its secondary character. In their normal course the amoebae by fermentative cytolysis invade the muscularis mucosae. The less pronounced the bacterial infection the more typical the amoebic lesions become. It was established that synergic infection was primarily brought about by haemolytic streptococci and that they were responsible for the bacterial spoiling, but later they were superseded by a pathogenic variety of *Bact. coli*. An associated trichomonas infection appeared to play no part. The bearing of these observations on the clinical picture in man should be critically assessed. *P. Manson-Bahr*

COUTELEN, F., BIGUET, J. & COCHET, G. Déterminisme de la phagocytose expérimentale de divers amidons par *Entamoeba invadens*. [**Experimental Study of Phagocytosis of Different Starches by** *Entamoeba invadens*.] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 11/12, 652–6. [15 refs.]

Cultures of *Entamoeba histolytica* are known to be most prolific when the medium contains rice starch ; other forms of starch are much less suitable. The phagocytosis of different starches by the reptilian amoeba, *E. invadens*, was compared, and rice, arum, oats, maize, arrowroot, barley, pea, wheat, rye and potato were studied. The size of the granules of these starches was measured. Unlike the human amoeba, the snake amoeba actively ingested all the materials, even the potato starch which was present in grains about 30–60 μ in diameter. These were the largest of all those tested and were least utilizable. It was remarkable that granules 32 μ in diameter could be ingested by organisms measuring themselves only 36 μ. Nevertheless, a preference was shown for the smaller types, *e.g.*, rice starch at 4–6 μ ; this also was found to possess the additional advantages of being regular in form and not liable to agglomeration. Arum starch also shows these properties and is equally effective in cultures of the organism.

The starch is stored as glycogen in the endoplasm of the amoeba, where its presence can easily be demonstrated by the use of Lugol's iodine solution.
P. C. C. Garnham

See also p. 641, ROBERTS, **A Protozoological and Helminthological Survey of Three Races in Nairobi, Kenya.**

LEPROSY

MAURANO, Flavio & others. **Tratado de Leprologia. Vols. 1–5.**

This book is reviewed on p. 678.

INNES, J. R. **Leprosy in Kenya.** *East African Med. J.* 1949, Feb., v. 26, No. 2, 32–5.

This study, carried out in the second half of 1948, followed the lines of the author's leprosy survey in Uganda [this *Bulletin*, 1949, v. 46, 263]. Detailed statistics are shown in two tables. In all, 53,814 persons were examined in seven main areas, including the coast, inland and highlands. The incidence of leprosy averaged 10·2 per thousand, the highest being the Nyanza area (31·7) and the lowest the Teita-Voi-Sagala area (0·9). The estimated number of cases in Kenya is put at 35,000. The Jaluo tribe were the most heavily affected and the Wateita, Kipsigis and Nandi the least. The author suggests that the course of spread is probably from West to East and not from the coast. The type of leprosy in Kenya is described as " something in between moderate and severe " : about 20 per cent. of cases are of the infectious lepromatous type and because of living conditions of the people a slow increase of the disease appears to be inevitable at present. The general observations are largely similar to those in the case of Uganda ; overcrowding and high humidity, especially the first, are influential factors in stimulating a high incidence of the disease : movements of the people and especially absorption of members of highly affected tribes into employment may enhance the spread.

Facilities for treatment and control are inadequate : only 50 to 60 cases are under effective modern treatment and some 200 others are in two leprosy camps. There is obvious scope for an active campaign with modern facilities and propaganda. *H. J. O'D. Burke-Gaffney*

AUSTIN, C. J. **Central Leper Hospital, Makogai (Annual Report 1947).** *Fiji, Legislative Council. Council Paper No. 40.* 1948, Appendix 6, 34–40, 1 diagram.

Dr. Austin's report on the Central Leper Hospital, Makogai, gives an informative account of the position during 1947, supported by 8 useful statistical tables and a diagram.

At the end of 1947 there were 703 patients in the hospital, an increase of 92 during the year : of these, only 19 were from Fiji itself and the remaining 73 came from neighbouring islands, principally the Gilbert Islands which contributed 45 patients to this increase.

New admissions amounted to 146, of which 64 were from Fiji and 82 from other South Pacific territories. It is noteworthy that 46 of the Fiji admissions were Indians and only 14 were Fijians. Furthermore, the number of Indian patients increased by 27 during the year and the Fijians decreased by 5 : the ratio of Indian to Fijian inmates at Makogai is indeed steadily increasing and is now well over 2 : 1, and 19 of the 46 Indian admissions are in fairly advanced and infective lepromatous stages, as compared with only 3 of the 14 Fijian admissions.

In fact, some 70 per cent. of the Indian patients are in the lepromatous stage which contrasts with findings in India, where the neural type largely preponderates. This situation in Makogai is further reflected in the fact that of 23 deaths, 9 occurred in Indians and that of 30 discharges only 10 were Indians. During the past 4 years, the annual discharge of Indians has only

once exceeded that of Fijians and the totals during that period have been 63 Fijian and 58 Indians, despite the great preponderance of the latter patients.

The epidemiological importance of these findings is discussed : as the Indians live more independent and less supervised lives, it is much more likely that undetected cases would occur among them.

Of the 52 admissions from the Gilbert Islands, 23 were fairly advanced and 16 were very advanced lepromatous cases : over 80 per cent. were infective. War conditions and enemy occupation would have caused deterioration in the position. The finding of 7 moderately advanced cases out of 9 Samoan admissions is more disturbing, and the author indicates the urgent need for special training of medical assistants in these islands who would be allocated to a travelling diagnostic survey, as has been done successfully in the Cook Islands where admissions are now among the earliest cases in Makogai.

Tables show in detail the distribution of cases in terms of nationality, types of disease and progress, the incomparably better outlook in early neural cases being obvious.

The Medical Superintendent took with him on visits to Samoa, Tonga and Niue Island a 16 mm. film dealing with Makogai and it was evident that this was greatly appreciated.

There were 8 deaths from tuberculosis, five of the patients being diagnosed during the year. The importance of this rapid development of the disease in those under fairly close medical supervision is stressed.

At the end of the year, 13 cases of tuberculosis remained : these had been confirmed by the tuberculin test, X-ray and sputum examination. Four of the patients were Gilbert Islanders, two each Indians and Fijians, and one each from other islands. Routine tuberculin tests and X-ray examinations are being made as far as possible, despite shortage of films and drugs. In 1947, a total of 266 X-ray examinations were made : 79 of these were of bony lesions.

An imposing list of items of food and other materials produced at Makogai in the year includes 840,000 lb. of vegetables, 99,858 lb. of bread and 39,126 lb. of beef. There were also 5,657 gallons of milk and 4,457 eggs. An interesting item is the production of over 9,000 lb. of soap.

The only major constructive work possible during the year was the erection of a new school building for the boys.

[This is an instructive account of an admirable institution : it is regrettable that post war difficulties should make delay in improvements and extensions inevitable.] *H. J. O'D. Burke-Gaffney*

DE SOUZA CAMPOS, Nelson & BECHELLI, Luiz Marino. **Sintomatologia nervosa da lepra.**

This book is reviewed on p. 681.

REYES, E., BARRIENTOS, E., RODRIGUEZ, J. J., CARRANZA AMAYA, A. & PERALTA, R. **Severe Reaction resembling Therapeutic Shock in Lepers following Administration of " Diasone ".** *Arch. Dermat. & Syph.* 1949, Jan., v. 59, No. 1, 118–19.

Two patients in San Salvador, aged 39 and 12 years, were treated for lepromatous leprosy, confirmed bacteriologically. After some months of treatment in 1946 with chaulmoogra oil, later replaced by promin, the nodular eruptions disappeared almost entirely.

In May 1947, diasone was introduced as a routine treatment in the authors' department and each patient was given " a daily dose of 0·3 gm. given three times a day by mouth ". After 8 weeks of such treatment, the two patients in

question complained that their former eruptions were again breaking out. Examination showed that nodules were spread over exactly the same areas which they had originally covered. This phase was accompanied by migraine, epiphora, nausea and fever. Diasone therapy was suspended and the phenomena disappeared gradually within 3 days. At the time of the appearance of the reaction, the patients had received 15·1 gm. and 10·4 gm. of diasone respectively.

It is added that two weeks later, diasone was given again to the first patient and the eruption reappeared within 4 days with greater intensity and took a longer time to disappear. Hence in such cases, diasone should be completely discontinued. The authors note that, although such reactions as vomiting, diarrhoea and allergic dermatitis have been recorded with the use of diasone, the present reaction appears not to have been described. They liken it to the Herxheimer reaction. *H. J. O'D. Burke-Gaffney*

CAPURRO, E. T. & GUILLOT, C. F. Vitaminoterapia D_2 a altas dosis en el tratamiento de la reacción leprosa tuberculoides. [**Treatment of the Leprous Reaction in Tuberculoid Leprosy with Vitamin D_2 in large Doses.**] *Rev. Argentina Dermatosifilologia*. 1948, July–Dec., v. 32, Nos. 3/4, 287–93.

Charpy has used pure vitamin D (Sterogyl 15) in alcoholic solution for lupus patients in doses of 15 mgm., three during the first week, two weekly for the next three weeks, and thereafter once a week till a year's treatment had been completed. The results were reported as striking (*llamativos*) ; the inflammation, oedema and erythema disappeared in a few days, and the nodules, though more resistant, became smaller and in time they also disappeared. Charpy explained its action thus : " Vitamin D_2 in large doses properly spaced with a diet not too acid and not too alkaline and with a proper amount of calcium creates in the tissues a state of permanent acidity. Apparently this tissue acidosis brings sterilization and cure of tuberculous lesions". *Myco. tuberculosis* and *Myco. leprae* being closely allied, the authors decided to try the same treatment in the acute reactional states of tuberculoid leprosy.

Five patients started the treatment in September, 1946. In four, the lesions began to improve within 7–21 days and they were cured [in the authors' words there was 100 per cent. improvement] in 45 days and the vitamin treatment was stopped in January, 1947, that is, after 4 months. One gave up the treatment because of intercurrent cardiac trouble.

Later, a fresh group of 10 patients came under observation ; eight kept up the treatment, which was modified somewhat from the original ; 600,000 units were given thrice weekly for 3 weeks. Details of one patient, a woman of 37 years, are given, with the remark that the others responded similarly. This patient had already been treated with chaulmoogra, the oil and the ethyl esters, and with promin and other drugs. Improvement began after 7 days and continued without set-back ; the nasal obstruction cleared in 3–4 weeks, the maculae lost their colour and desquamation was copious. [There appears to be some confusion about the dosage in units. In one place it is stated that the patient took three ampoules in the week, " total 180,000 units ". If the dose was an ampoule of 600,000 units this total should be 1,800,000. Later, it is said, another three ampoules were taken, or " altogether 6 ampoules of 360,000 units " (? 3,600,000). Three more in the third week, that is, " a total of nine ampoules or 5,400,000 ", which is correct. Altogether in the first month " there were given eleven ampoules of 6,660,000 units " (should be 6,600,000). During the second month " one ampoule a week. Total four ampoules or 720,000 units " (this should be 2,400,000 units).] *H. Harold Scott*

Ann. Intern. Med. 1949, Mar., v. 30, No. 3, 692–700. [27 refs.] **New Developments in the Management of Leprosy.**

A useful review.

de Souza Campos, Nelson & Bechelli, Luiz Marino. **Organização e Funcionamento de Preventorios.**

This book is reviewed on p. 682.

HELMINTHIASIS

Roberts, J. I. **A Protozoological and Helminthological Survey of Three Races in Nairobi, Kenya.** *J. Trop. Med. & Hyg.* 1949, Mar., v. 52, No. 3, 49–59, 2 charts.

This is a record of seven years' routine examinations of stools of people living in Nairobi, Kenya. The specimens came from in- and out-patients (European, Asian and African) and were examined direct and after centrifugation, in saline and iodine-stained preparations: 33,166 European specimens, 40,503 African and 5,409 Asian were examined. More than half of the European and three-quarters of the African specimens showed the presence of parasites. Helminthic infections were light and the cases were regarded more as carriers than as victims. There were few symptoms and little or no anaemia. Nevertheless, the author suggests that the mild toxaemia arising from the infections is of major importance in causing an almost life-long damage to the power of development, leading to general mental and physical apathy. The backwardness of tropical populations is said to be associated with this toxic absorption. [Unfortunately no proof of toxaemia or of its direct relation to these conditions of apathy is presented. The fact that the mental and physical powers of newly-recruited African technicians improve after anthelmintic treatment, may easily be ascribed to changes in environment, better food, etc.]

Schistosomiasis is ranked high as a cause of ill-health (1·6 per cent. of all specimens contained ova); *S. mansoni* infections are found from the coast to 8,000 feet above sea-level. No collections of water in inhabited areas of Kenya can be regarded as free from the possibility of infection. The chief molluscan host is *Biomphalaria pfeifferi*; another is *Bulinus tropicus*. Other important helminths were *Taenia saginata* (9·0 per cent.), *Ascaris* (4·3 per cent.), and *Necator americanus* (5·3 per cent.).

Entamoeba histolytica is essentially found in town-dwellers; it is rare in rural areas. The incidence of the infection is highest in the hot dry season. It is more commonly associated with mild symptoms of abdominal discomfort than with dysentery. In the latter case, the vegetative forms are said to be always larger than in the former. For a year, cases were classified according to the presence or absence of ingested red blood cells in the amoebae—there were only two cases with ingested cells and 80 without. *Giardia intestinalis* was the cause of a chronic mucous diarrhoea in both adults and children. Six cases of balantidial dysentery were encountered. A survey of 86 intestines from pigs slaughtered in the Nairobi abattoir showed that 32 per cent. were infected with *Balantidium*. In the main table, 79 cases of *Isospora hominis* are recorded, without comment. [In view of the comparative rarity of this infection, as indicated in the literature, it would have been an advantage if some amplification of this interesting finding had been given in the text.] *P. C. C. Garnham*

Osorio, M. Teresa. Sobre una modificación a la tecnica de cuenta de huevecillos de Stoll. [**A Modification of Stoll's Method for counting Helminthic Ova.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1948, Sept., v. 9, No. 3, 245–52.

For his experiments the author used puppies 2–6 months old and infected them with *Ancylostoma caninum*. His modification of the Stoll method is slight, but he claims that it is quicker, easier in not needing any special chemicals, can be carried out by any practitioner and is practically as accurate. He places 1 gm. of faecal matter in an Erlenmeyer flask, adds water to the 30 cc. mark and 10 glass beads, inserts a rubber stopper and shakes well to obtain a homogeneous suspension; he extracts 0·1 cc. with a capillary pipette, places it on a slide with a coverglass 20×40 mm. and counts all the eggs in the preparation. He repeats this with a second sample and multiplies the total result by 200 to obtain the number of ova in 1 gm. of faeces. The difference from the classical Stoll's method consists in adding water instead of decinormal soda and diluting 1 : 30 instead of 1 : 15. He made 244 countings by the methods of Stoll, Lane, Caldwell, and this modified Stoll and shows in tables that the results obtained by his modification are readily comparable with and closely similar to those with the original Stoll and on the whole better than with the Lane or Caldwell methods. *H. Harold Scott*

Bonilla Naar, A. & Gómez Vargas, M. "Aex" y faux [Faust] simplificado. Dos nuevos metodos para investigar parasitos intestinales. [**The AEX Method and Faust's Method (Simplified) for detecting Intestinal Parasites.**] *Repertorio Med. y Cirugia*. Bogota. 1948, v. 4, No. 1, 49–68. [48 refs.]

These two procedures are detailed and the authors then compare the results obtained by these and the standard methods of Willis-Mallory and the Stoll techniques and direct examination.

By the AEX method of Loughton & Stoll, 56 cc. of tap water are placed in a Stoll flask and 4 cc. of faeces emulsion in water added; the whole is vigorously shaken with glass beads to obtain a homogeneous product; 1·5 cc. of this is placed in a 15 cc. centrifuge tube and to this are added 3·5 cc. of 20 per cent. HCl; after stopping with a rubber plug the mixture is shaken for one minute, then put aside for two minutes. Next, 5 cc. of a mixture of ether and xylol in equal parts are added and the whole is again shaken for one minute and centrifuged at 1,800–2,000 r.p.m. for two minutes. The material collected on the walls of the tube is carefully removed by a thin piece of wood, the supernatant is poured off and one drop of decinormal NaOH added to the deposit; some of this deposit is removed with a capillary pipette and examined.

The original Faust method, say the authors, is inconvenient in needing several manipulations and is time-wasting. The first-named author, Dr. Bonilla Naar, has modified it thus: He mixes about 1 gm. of faeces in 10–12 cc. of zinc sulphate solution, sp. gr. 1,180 in 15 cc. centrifuge tube and centrifuges for a minute at 1,500–2,000 r.p.m. With a capillary pipette or a loop material is taken from the surface, placed on a slide and examined.

The authors give the results of 100 samples examined at their laboratory by each of the five methods and conclude:

1. The *AEX method* was the best for finding ova of hookworm, *Trichuris*, unfertilized *Ascaris* and larvae of *Strongyloides stercoralis*. By it also cysts are found, but mostly so changed as to present difficulties in identification.

2. The *Simplified Faust method* is of less service for helminthic ova, but is the method of choice for protozoal cysts.

3. The *Willis-Mallory method* was good for concentrating helminth ova, but not so good as AEX because unfertilized *Ascaris* does not show up and neither larvae nor cysts were found by it.

4. *Stoll's original method* was useful for helminth ova and larvae, but less so than AEX or the Willis-Mallory.

5. *Direct method* was the only one to show trophozoites of *E. histolytica* in acute amoebiasis and in only 50–70 per cent. were helminthic ova found; in 43 per cent. *E. histolytica* and in 83 per cent. *Giardia intestinalis* were found.

" In none of our preparations did we meet with ova of *Enterobius vermicularis* which confirms the rarity of this in the faeces [here] and the need for using Hall's Cellophane method or some modification of it." *H. Harold Scott*

Neves, A. de O. A esquistosomóse no Estado do Espírito Santo. [**Schistosomiasis in the State of Espirito Santo.**] *Anais Depart. Estadual Sáude Espírito Santo.* 1948, 37–102, 5 maps & 1 chart.

After remarks upon the geographical situation, the climate, the hydrographic and other general details of this State of Brazil, the author gives the results of examinations carried out in 18 localities of Espirito Santo. In the majority of them only 100 or so examinations were made and in some much less, so that detailed figures will have little interest. Summing up the examinations of 56,206 faecal specimens in the course of 10 years, 1935–1944, 800 were positive (1·4 per cent.). This, however, is regarded as misleading if applied too strictly, for in another set of examinations, among 6,159 there were 759 positive, or 12·3 per cent. and at Guandu and Santa Joana, the most severely infested zone, an even higher degree was found, 643 among 2,893 (22·2 per cent.). The vector is *Australorbis centimetralis*. *H. Harold Scott*

Erfan, M., Erfan, H., Mousa, A. M. & Deeb, A. A. **Chronic Pulmonary Schistosomiasis: a Clinical and Radiological Study.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Mar., v. 42, No. 5, 477–85, 6 figs. on 4 pls. [10 refs.]

From 103 parasitically diagnosed cases of urinary and intestinal schistosomiasis at the Fouad I Hospital in Cairo 49 cases of pulmonary schistosomiasis were selected for study. The diagnosis rested on the fact that the patients had a proven gut or bladder infestation, and radiological changes in the lungs which improved after antimony treatment. Forty-four of the patients were males and the rest females; this sex-disproportion is in part due to the reluctance of women to enter hospital; the ages of the patients ranged from 10 years to 55 years (children below 10 are not admitted to this hospital).

The onset of symptoms was insidious; those commonly encountered were dyspnoea on exertion, cough (and in one case slight haemoptysis), general weakness, giddiness and fainting, palpitation, and thoracic and praecordial pain.

In 34 of the 49 patients no physical signs were found in the lungs; in 15 there were some moist sounds at the bases; sputum was examined from only 7 of the patients, and in no case were schistosome ova found in it. The physical signs included slight cyanosis (3 cases), clubbing of the fingers (7 cases), and swelling of the superficial cervical veins with congestive heart failure (2 cases). In 28 of the 49 patients there were signs of pulmonary hypertension and dilatation; in most there was accentuation or splitting of the second heart sound and a harsh systolic murmur in the pulmonary area. Forty-one patients had enlargement of the liver, and 38 enlargement of the spleen; 10 had ascites, and 5 oedema of the legs. No patient had a pyrexia due to the schistosomal

pulmonary involvement; the haemoglobin values ranged from 15 per cent. to 104 per cent., but in 6 cases the low figure was ascribed to ankylostomiasis; the eosinophil counts ranged from 1 to 40 per cent.

Antimony treatment (the drug used is not specified) of 44 of the patients resulted in improvement in some cases, but it caused fever, urticaria, acute pulmonary congestion and a marked eosinophilia in others, one of whom died as a result. The pulmonary reaction to specific treatment may be due to allergy or to focal reactions around the lung lesions. Bronchial asthma and a focal pneumonia, possibly verminous, are their clinical manifestation.

Erfan and Deeb, in an appendix, classify the pulmonary lesions into three radiological grades: Grade I, in which there are focal arterial changes; Grade II, in which there are widespread arterial changes with slight heart changes; and Grade III, in which there are widespread arterial changes with gross heart changes. They detail the lesions they encountered and give illustrative radiographs. *A. R. D. Adams*

GELFAND, M. **Schistosomiasis of the Female Genital Tract.** *South African Med. J.* 1949, Apr. 2, v. 23, No. 14, 255–7.

The author reviews the literature of schistosomiasis of the female genital tract and refers to the difficulties in interpreting correctly symptoms attributable to infections of that tract; many parts of the genito-urinary tract may be affected by schistosomiasis concurrently and, particularly in Africans, the prevalence of coincident gonorrhoea or other infections may complicate the issue.

Existing literature does not appear to define clearly how frequently the different parts of the genital tract may be affected. The present study, made in Southern Rhodesia, was directed towards determining this point and also the relative frequency with which *S. haematobium* and *S. mansoni* respectively settled in these parts.

Thirty African women between 20 and 35 years were studied consecutively at autopsy: evidence of schistosomiasis was found in each case in either the urinary or intestinal tract. The various organs or parts were dissected and separated carefully and placed in appropriately labelled containers. Each was digested separately for 12 hours at 60°C. in 10 per cent. caustic potash solution and the digested portions were examined microscopically for ova.

The results are given for the bladder, rectum, vagina, cervix, uterus, ovaries and Fallopian tubes. The bladder and rectum contained ova in every case. In one case the bladder contained ova of *S. mansoni* in addition to *S. haematobium*. In ten cases, the rectum contained ova of both species, in 18 there were only *haematobium* ova and in 2, *mansoni* ova alone.

The distribution of ova in the genital tract of the 30 cases was as follows: —

Number of cases	Number containing only a few ova
Vagina—29	7
Cervix—28	11
Uterus—25	(not stated)
Ovaries—24	10
Fallopian tubes—16 ...	6

It will be noted that, in the majority of positive cases, ova were present in fair quantities, the minority reporting "a few ova only".

In every case *S. haematobium* was found: in only one of the 12 having *S. mansoni* in the rectum were ova of this species found in the genital tract; this was in the vagina where *mansoni* ova were found in addition to *haematobium* in a single case. The author draws attention to this frequency of ova in the genital tract in *haematobium* infections and their rarity in *mansoni* infections: "It may be assumed that if a patient has urinary bilharziasis, the probability is that she will have ova of *S. haematobium* in some portion of the genital tract". In no case in this series was a genital tract free from ova and generally more than one part was affected. It is noted that the vagina and cervix were most commonly affected.

The author points out that the exact significance of these findings cannot be assessed: but "it seems reasonable to argue that in the majority of cases the damage is minimal and symptoms will not be produced, but where the local deposition is severe, particularly in the Fallopian tubes or ovaries, effects from the fibrosis may ensue, resulting in sequelae, such as sterility or ectopic gestation". *H. J. O'D. Burke-Gaffney*

Talaat, S. M. & Shoaib, S. **The Intensive Treatment of Schistosomiasis with Tartar Emetic.** *J. Roy. Egyptian Med. Ass.* 1948, Dec., v. 31, No. 12, 961–3.

The authors have continued the work already reported [see this *Bulletin*, 1948, v. 45, 719]. They have treated 90 hospital patients having schistosomiasis (17 of them under 15 years of age) with intensive courses of tartar emetic [species of schistosome not stated]. Each adult patient received 2 grains of tartar emetic dissolved in 20 cc. of 5 per cent. glucose twice daily on two consecutive days. As the first five children did not seem to respond to this course, the remainder were given "three injections instead of two" [later it is stated that "children under 15 years of age must be given an extra injection on the third day to ensure satisfactory results". There is some ambiguity in the use of the word "injections" which seems in some of the contexts to mean "daily dosage": the exact amount of tartar emetic given to children is not therefore clearly stated].

Patients were observed for one month, and in a few cases for two to seven months. At the end of the observation period, 73 patients were rid of their ova, two passed dead ova and 15 passed living ova. One month later 10 of these 15 were given a second course and all (with the exception of one child) became free from ova.

The authors state that their modification of injection technique "did not seem to affect or increase the untoward reactions when individual tolerance was observed".

Since the paper noted above was published the authors have found that renal disease does not contra-indicate this form of therapy, so long as urinary output is good: they have also given the course to two patients having a haemoglobin percentage of 25 to 30. There were no complications, but nevertheless the authors consider administration of the drug risky in such cases. A decompensated heart and cyanosis are to be considered contra-indications.

Ten of twelve children under 15 who were given the additional treatment ceased to pass ova.

One of the authors has treated 13 private patients without complications. In these cases, the patient rested for 15 minutes before leaving the clinic and was advised to abstain from manual work for a week.

In the hospital cases, the patients were injected with a S15 or 16 bore needle: the patient lay flat during the injection and for 10 minutes afterwards.

H. J. O'D. Burke-Gaffney

SCHUBERT, M., GOLDBERG, Evelyn & SCHREIBER, Freda G. **Comparison of Several Antimonials in the Treatment of Experimental Schistosomiasis Mansoni in Mice.** *Amer. J. Trop. Med.* 1949, Jan., v. 29, No. 1, 115–27.

The results of screening tests with various drugs in mice infected with *Schistosoma mansoni* have already been reported in detail by SCHUBERT [this *Bulletin*, 1948, v. 45, 620, 621]. Comparable dosage of the different substances was taken as that approaching the maximum tolerated. A large-scale attempt has now been made to determine the therapeutic indices of the antimonials used against this infection by direct comparison of the LD_{50} and CD_{50} (the dose that cured half the mice). Difficulty was found in assessing accurately the LD_{50}. It was determined on infected mice under the same conditions as those in the treated groups, and required consideration of the death rate among infected but untreated controls. The mice were infected by intraperitoneal injection of 150 cercariae and the worms were allowed to mature for a period of 8 weeks. During the following 2 weeks, groups of 15 mice were treated daily on 6 successive days with various antimonials by intraperitoneal injection, except in the case of butyl antimonyl gallate which was added to the diet. Two weeks later, *i.e.* at the 12th week after infection, the mice were autopsied and the number, state and distribution (antimonials cause the worms to migrate from the mesenteric veins to the liver) of the worms were determined. Sodium antimony tartrate, and urea stibamine appeared to be without effect, but neostibosan and neostam had some effect on the worms at maximal dosage. Their therapeutic indices were below 1. Fouadin and trithiosorbitol showed activity with indices about 1. Three antimony tri-(thiomercaptides) of the general formula $Sb(SR)_3$, soluble in peanut oil, possessed considerable activity as did butyl antimonyl gallate, and their therapeutic indices ranged from 2 to 3. Some interesting experimental data are also given which indicate that there is an increase in death rate of the infected mice with advance of the infection. So far as these results in mice go, they indicate that some of the Sb compounds described here are more effective against the infection than those generally used. *J. D. Fulton*

AZIM, M. A. & AYYAD, N. **A Preliminary Report on the Value of Palm-Leaf Traps in the Survey and Treatment of Streams infested with Snails.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Nov., v. 42, No. 3, 231–46, 9 figs. & 1 graph.

The authors describe in detail the experiments they made with palm-leaf traps in the control of snails in the streams of Egypt. They wished to know to what extent, and at what level, snails are carried by large streams; what proportion will be caught by the traps in the presence or absence of other foodstuffs; and what is the distribution of snails in a stream under various conditions of current, depth, etc. They have illustrated the paper by attractive line drawings of the palm-leaf traps in position.

The traps are made of palm leaves chained together in parallel. Each rung consists of two superimposed palm leaves pointing in opposite directions, and about 2 metres in length, and the rungs are about 50 cm. apart. Some 10–13 rungs chained together form the traps, and the lowest are weighted so as to reach the bottom of the stream, or hang down into it. The force of the current bulges the traps, sometimes very greatly. Snails seek the palm leaves, which present a large surface on which they feed or deposit eggs. For finding snails, these traps are better than nets or the process of dipping.

The results of several experiments in flowing water showed that most of the *Bulinus* snails caught were found near the surface of the water or about the middle of the traps, and that these snails tended to collect where the water

was fairly shallow and the current moderate. The traps functioned well even in the presence of natural food supplies (weedy vegetation) of the snails. In shallow, slow-flowing canals the snails tended to collect on the slopes of the sides, or on the bottom, but in swifter streams they were usually confined to the slopes, and avoided the more swiftly moving water.

In ponds, palm leaves stuck into the banks and projecting into the water collect snails readily, and if they are renewed each week, will greatly reduce the number of snails within a month. Streams may be treated in the same way, but it is advisable to clear the weeds first, and then to stick the leaves into the banks, below the water surface, about 1 metre apart. In this method they are not chained together as in the traps described above. One man can attend to 3 kilometres of bank, removing and replacing the leaves and collecting the snails from them, every week. This method may be used where closure of the canals, and treatment by copper sulphate, are not possible. Certain streams have been so treated for long periods, with good results. [See also this *Bulletin* 1947, v. 44, 97.] *Charles Wilcocks*

Cawston, F. G. **Mechanical Purification of River Water.** [Correspondence.] *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Mar., v. 42, No. 5, 507–8.

In this note, examples are given to show the reduction of coliform bacteria in water which takes place as a result of pumping to raised tanks; and the author considers that "the chances of contracting schistosomiasis are much reduced when water is pumped through metal piping, especially where it is passed through more than one tank and drawn from the bottom layer rather than the surface which harbours those cercariae which attack man".

Flowing water tends to purify itself by contact with stones and by passing over waterfalls: but vegetation and molluscs tend to accumulate below waterfalls and to reinfect the water. *H. J. O'D. Burke-Gaffney*

Biaggi, N. & Pirazzi, R. **The Effect of Chloramine on the Miracidia of** *Schistosoma mansoni*. *Puerto Rico J. Pub. Health & Trop. Med.* 1949, Mar., v. 24, No. 3, 246–50. [Spanish version 251–5.]

"1.. Concentrations of chloramine in water, varying from 0·3 to 0·89 parts per million, had a definite effect on the viability of the miracidia of *S. mansoni*.

"2. Chloramine concentrations of 0·45 parts per million inactivated miracidia in an average time interval of 7·2 to 8 minutes.

"3. Miracidia lost their motility in chloramine concentrations of 0·89 parts per million in the maximal time period of five and a third minutes."

Kuo Shao Chou, Yui Huan Wen & Chang Chiang E. **An Abbreviated Report on Field Survey of Schistosomiasis in Szechwan.** *Chinese Med. J.* Chengtu Edition. 1945, Apr., v. 63A, No. 3, 144–8.

In 1943 an autochthonous case of *Schistosoma japonicum* infection was found in Chungchingchow, Szechwan, and in 1944 the authors made a survey of that area, and 4 other places round Chengtu, to find other cases; they give details of the people examined, but they did not find any new cases. They also examined over 1,000 snails (*Katayama*), but with negative results. In the mesenteries of 2 of 30 cattle *S. japonicum* was found, but 6 buffaloes and 1 goat were negative. The cattle were heavily infected with *Ornithobilharzia* species.

S. japonicum infection, therefore, is slight round Chengtu. This may be a reflection of the farming practices, for only in summer is the land submerged

for the cultivation of rice, and the molluscan hosts, therefore, have only half the year to propagate themselves and to receive and transmit infection.

Charles Wilcocks

Best, A. E. & Wu, D. C. **Schistosomiasis on the Chengtu Plain.** *Chinese Med. J.* Chengtu Edition. 1945, Apr., v. 63A, No. 3, 139–42.

Until 1939, schistosomiasis had not been reported from the Szechuan province of China : thereafter, hatching tests were done on stools of suspected cases and in five years, 15 cases were collected. In one case, the miracidium was found only after the 10th hatching test, and it is suggested that the disease is probably not as uncommon in the province as had been supposed.

The ages of the patients were from 12 to 40 years and all but one were males, either farmers or country school children. The disease was found along the tributaries of the Yangtze around Chengtu.

The clinical features are listed : the prominent manifestations were splenomegaly, anaemia, enlarged liver, fever and leucopenia, with eosinophilia. Urticaria was present in only two cases. Other tables show the measurements of spleen and liver and the laboratory findings. It is noted that in the acute stage, leucocytosis was commonly present.

The patients were treated with injections of antimony potassium tartrate, varying in dosage according to the patients size and reaction : a sudden drop in the leucocyte count was taken as an indication for immediate suspension of the antimony injections.

The authors believe that many of those affected contracted the disease early and that the intestinal manifestations had passed unnoticed.

H. J. O'D. Burke-Gaffney

Koenigstein, R. P. **Observations on the Epidemiology of Infections with** *Clonorchis sinensis*. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Mar., v. 42, No. 5, 503–6, 1 fig.

Acute clonorchiasis is rarely seen, possibly because Chinese (Cantonese) and Japanese contribute the great majority of cases and, having harboured the infestation for centuries, they have perhaps developed some degree at least of racial immunity. Hence this account of an acute outbreak on a large scale among nearly 20,000 persons of European origin gathered together in Shanghai under poor hygienic conditions is of no little interest. Helminthiasis was very prevalent ; nearly half of the subjects had ascariasis, about one in five had bacillary dysentery and one in ten amoebic dysentery and giardiasis.

The origin of the outbreak, which took place in February and March, 1946, was pickled fresh-water fish sold as herrings and eaten avidly ; 20 to 30 per cent. of the displaced persons were affected. The clinical picture was that of an acute infection : malaise, chills, fever up to 40°C., subicterus, enlarged and tender liver, eosinophilia from 10 to 40 per cent., in one patient 88 per cent. Faecal examination was positive only after 3–4 weeks, the first symptoms being probably due to invasion of the biliary passages by metacercariae. After a few weeks the acute symptoms subsided, but general malaise and an eosinophilia of 5–10 per cent. remained.

The infestation seemed to pave the way for other intestinal infections, for *Giardia intestinalis* and *E. histolytica* increased also almost *pari passu* ; over 3,500 faecal examinations were made in 16 months.

Treatment was not very satisfactory. Gentian violet seemed to give some relief, and combined treatment with emetine, yatren, carbarsone and atebrin [mepacrine] might be successful. Antimony compounds proved very disappointing.

H. Harold Scott

Tillman, A. J. B. & Phillips, H. S. **Pulmonary Paragonimiasis.** *Amer. J. Med.* 1948, Aug., v. 5, No. 2, 167–87, 4 figs.

The authors give a short systematic account of paragonimiasis, and refer to the special features that were noted in twelve cases among Filipino guerrillas in a hospital in Leyte.

In five patients, the first onset of symptoms was associated with a febrile attack which was probably malaria: when the fever subsided the lung symptoms, cough and haemoptysis, remained and developed. The cough was dry at first but rapidly became productive, with 30 to 90 ml. of sputum, which was usually "gelatinous, purulent, bloody and of a slightly sour odour in which were scattered dark brown flecks resembling cigarette tobacco shreds". Ova were found in such sputum. The cough tended to be worse after exertion and at night. Most patients had chest pains. Dyspnoea was associated with pleural effusion in three patients. Two patients complained of pain in the extremities.

Despite the symptoms most patients seemed relatively well. Physical signs were present in the lungs at some time in every patient—fine to coarse râles in varying portions of the lungs. "Characteristic signs" of fluid were noted in two patients, but fluid was apparently present in four cases. An enlarged liver was found in three cases.

Ova were found in sputum, faeces and pleural fluid. They were found—sometimes not until the 10th examination—in the sputum in all cases, in the faeces in four cases (7 times in a total of 71 stool examinations), and in the pleural fluid in one case.

The significance of the blood findings was not clear since all had multiple parasitic infections. Eosinophilia was constant: in one case only (maximum 8 per cent.) was the percentage consistently less than 12 and the maximum was 56. The blood sedimentation rate was above 20 mm. in 10 cases. In four there was a reversal of the albumin/globulin ratio and in all but two it fell below 2·0. The formol-gel test was positive in two cases.

Radiological changes were present in every case; there were either massive areas of density, or diffuse, small, soft and usually multiple lesions. Both lungs were involved in five patients: the right lung and the lower lobes were most frequently involved. The lesions diminished during treatment in five cases, disappearing in three.

Tartar emetic was given intravenously in 4 cases; it was badly tolerated and had little effect. Emetine hydrochloride was thereafter adopted as the treatment of choice. Daily injections of 0·06 gramme for 8 or 9 days was the usual course. Symptomatic relief occurred in nine cases, usually after the first few injections. Constant absence of ova was noted in three cases after repeated courses of emetine. The twelve case reports are given in detail. [The paper contains much other valuable data, but the reader may be prejudiced by the fact that Sir Patrick Manson is referred to twice as Mason.] *L. E. Napier*

Kouri, P. Diagnostico, epidemiologia y profilaxis de la fascioliasis hepatica humana en Cuba. Sindrome eosinofilico febril. [**Diagnosis, Epidemiology and Prevention of Human *Fasciola hepatica* Infection in Cuba. The "Febrile Eosinophilic Syndrome".**] *Rev. Cubana Lab. Clin.* 1949, Jan.–Feb.–Mar., v. 3, No. 1, 12–32, 8 figs. [57 refs.]

A general review of the subject with illustrations of technique.

See also p. 677, Saunders, **A Survey of Helminth and Protozoan Incidence in Man and Dogs at Fort Chipewyan, Alberta.**

Kuitunen-Ekbaum, E. **A Case of *Dipylidium caninum* in a Child.** *Canadian J. Pub. Health.* 1949, Mar., v. 40, No. 3, 115–16.

Halawani, A., Baz, I., Hafez, A. & Shawarbi, M. K. **Treatment of Tape Worms with Atebrine.** *J. Roy. Egyptian Med. Ass.* 1948, Dec., v. 31, No. 12, 956–60.

There is no drug which is completely satisfactory for the treatment of a tapeworm infestation. Success in treatment depends on the proper preparation of the patient by complete abstention from solid food for 48 hours, and proper clearance of the bowel, before the administration of the vermifuge.

A dose of atebrine [mepacrine] of 15 mgm./kilo of body weight given in gelatin capsules or coated tablets, after proper preparation, followed within a couple of hours by 1 to 2 ounces of castor oil, or by a large dose of magnesium sulphate, proved effective in removing entire worms with heads from 35 of 53 patients so treated. These worms proved to be both *Taenia saginata* (about 50 worms) and *T. solium* (5 worms). Most worms were evacuated on the day of treatment, but one was passed complete with head on the seventh day after it. The failures, in many cases, were probably due to inadequate preparation of the patient before administration of the drug.

Two patients suffered from toxic side effects in the form of vomiting, in both cases ascribable to excessive absorption of the drug. *A. R. D. Adams*

Pérez Fontana, V. Origen, desarrollo y extensión de la hidatidosis en América. [**Origin, Development and Extension of Hydatidosis in America.**] *Bol. Oficina Sanitaria Panamericana.* 1949, Feb., v. 28, No. 2, 124–56, 1 fig., 4 graphs & 10 charts. [14 refs.] English summary.

The English summary appended to the paper is as follows :—

" The report is written in two parts : First, a brief study is given on the biology and morphology of the parasite, etiological agent of the disease (*Taenia, Echinococcus granulosus*), its anatomic discussion and the systemic reactions produced. In the second part the author reviews, historically, geographically and epidemiologically, the development and extension of the hydatid disease in the South American Continent. The disease was probably introduced to America by dogs brought by whalers who settled on both banks of the River Plate, and it extended slowly to the neighboring countries. Charts and illustrations are presented, showing the extension of the disease among cattle and men. Epidemiological and ecological considerations are made with regard to the factors which determine the extension of the disease in the American Continent."

See also p. 664, Lehmann, **Macrocytic Anaemia in Central Africans in relation to Ancylostomiasis and other Diseases.**

Napier, L. E. *Strongyloides stercoralis* **Infection. Part I.** *J. Trop. Med. & Hyg.* 1949, Feb., v. 52, No. 2, 25–30, 1 fig. **Part II. Strongyloidiasis among Ex-Prisoners-of-War.** *Ibid.* Mar., v. 52, No. 3, 46–8.

i. British workers have regarded human strongyloidiasis as of minor clinical significance, but American workers have attributed significant pathological potentialities to it. The author now shares their view, and has been

further confirmed in it by his observations on ex-prisoners-of-war from the East. *Strongyloides stercoralis* infection, like hookworm infestation, occurs widely throughout the humid tropics; Indo-china, Siam, Burma, and Assam are among the areas of the world most heavily infected.

The life cycle of *S. stercoralis* is characterized by extraordinary variation. The normal infective stage of the parasite is the filariform larva; this develops from the rhabditoid larva outside the host, penetrates the skin or mucosal surfaces, reaches the blood stream and is carried to the lungs, where it penetrates into an alveolus. Here a mature male or female may develop; but more commonly this development occurs only after the larva has migrated up the respiratory passages and descended the alimentary tract to the small intestine. The gravid females, in the mucosa of a bronchus or the mucosa of the gut wall, deposit eggs which rapidly hatch rhabditoid larvae. The larvae deposited in the gut wall normally escape to the exterior in the faeces there to undergo an exogenous cycle, but they do not always so escape. They may remain in the tissues, reach the blood stream and recommence the cycle (direct endo-autoinfection), changing through the filariform stage to the adult in the process. Alternatively they may pass down the gut and develop to filariform larvae within the lumen of the bowel, to repenetrate it at a lower level and so continue the cycle (indirect endo-autoinfection). Again, the larvae may develop to the filariform type in faecal matter contaminating the perianal skin, and repenetrate the skin without undergoing an exogenous cycle (exo-autoinfection). By any of these means the worm infestation of the host may be increased without an exogenous parasitic cycle having taken place, a phenomenon which is unique in helminth infestations.

The exogenous cycle is also subject to variation. The rhabditoid larvae voided in faeces on reaching soil may become filariform and remain as such, now being infective; or they may develop to free-living adult males and females and undergo several such cycles while living in soil.

In view of the variations which may occur in the cycle in man, repeated stool examinations over some weeks may be necessary for the detection of an infestation.

The administration of the usual anthelmintics designed to destroy the parasites in the lumen of the gut is unlikely to be effective, as the worms are located parenterally for most of their parasitic lives.

The pathological lesions due to *S. stercoralis* occur at the chief sites of activity of the worm, *viz.*: (1) at the point of entry into the skin, (2) in the lungs and bronchi, and (3) in the intestinal mucosa. Petechial haemorrhages with local inflammatory changes occur at these sites, and the symptoms may be acute and of short duration, or chronic. In heavy infections of the gut there may be extensive sloughing, and ulceration may follow secondary bacterial infection; rarely, ileus or gangrene may follow penetration of the muscularis mucosae by larvae when direct or indirect endo-autoinfection occurs on a large scale. While infections in some cases are symptomless, more commonly there are indefinite digestive disturbances and ill-health, subject to periodic exacerbation. There is almost invariably eosinophilia (8 to 25 per cent.) and moderate anaemia. The stools of any patient from a known endemic area, who has suggestive symptoms and eosinophilia, should be thoroughly and repeatedly examined for larvae.

Treatment is unsatisfactory, and gentian violet by the mouth and antimony parenterally would logically appear to afford the greatest hope of destroying the parasites. In practice they have proved of doubtful value. Eventual spontaneous cure occurs as a rule, although the infection may persist for years.

ii. Strongyloidiasis is common among ex-prisoners-of-war from the Far East; at least 90 per cent. of those infected acquired their infections in Siam,

where it is estimated that between 25 and 100 per cent. of the men working on the railway were infected. The symptoms complained of are usually vague and mild, but often are associated with periodic watery diarrhoea. An outstanding and exceptional manifestation, however, was a periodic transient urticarial eruption first occurring within 12 inches of the anal orifice and often extending to the trunk or thighs. In many cases it resembled the creeping eruption due to *Ancylostoma braziliense*, and its linear progress could be followed over a considerable distance at the rate of an inch in ¼ to 1 hour. In other cases transitory urticarial weals appeared. Eosinophilia increased during the urticarial attacks. The attacks have recurred, though at increasing intervals, in some patients over a period of three years' observation. Apart from a few cases which have cleared up with large doses of antimony or of gentian violet, treatment has proved disappointing. The intensity of the gut infections in these men on the whole has diminished, and there has been no solid evidence of increased worm load due to auto-infection in any case.

The association between these skin manifestations and a strongyloid infection acquired in Siam is 100 per cent. Periodic petechial, urticarial, or linear eruptions with a " bathing drawers " distribution in ex-prisoners from Siam have invariably been followed by the discovery of strongyle larvae in the stools. The limited geographical area from which men suffering from these peculiar skin lesions were drawn suggested that a distinct species of *Strongyloides* might be responsible ; there was no morphological evidence on examination of the parasites that this was the case. The origin of the eruptions may be (1) penetration of the skin by rhabditoid larvae (exo-autoinfection) ; (2) migration of larvae entering the skin (exo-autoinfection), or even the gut (endo-auto-infection) near the anus ; (3) allergic reactions precipitated by the periodic systemic migrations of worms ; or (4) an unassociated infection acquired in the same area. The second explanation seems the most satisfactory, in view of the creeping nature of the eruption in many cases, but in no case has a larva been recovered from the lesions. *A. R. D. Adams*

CAPLAN, J. P. **Creeping Eruption and Intestinal Strongyloidiasis.** [Memorandum.] *Brit. Med. J.* 1949, Mar. 5, 396.

Creeping eruption resulting from exposure to the larvae of certain hookworms is well recognized.

In January, 1946, the author noted the occurrence of tortuous urticarial weals in ex-prisoners-of-war from the Far East. These weals usually started on the buttocks and extended upwards towards the iliac crest, on to the abdomen and back and down to the middle of the thighs. The lesions were very irritable. They moved at a speed of 5–10 cm. per hour : this is a far greater speed than is usually described for creeping eruption. The eosinophil counts were usually between 700 and 2,000 per cmm. (10–25 per cent.).

The first man in whom this was observed had worked on the Siam-Burma railway and had both a hookworm and a strongyloid infection. The former infection responded to treatment, but the latter did not, and the creeping eruption persisted. The author observed that this creeping eruption was almost exclusively confined to men who had been prisoners-of-war in Siam ; he found the condition in several hundred of them, and in over 98 per cent. he was able to demonstrate a bowel infection with *S. stercoralis*. The identity of the species was confirmed by Professor Buckley. It has so far not been possible to demonstrate strongyloides larvae in the lesion and even " presumptive proof is lacking, as it has been impossible to find any method of treatment which will eradicate the intestinal strongyloidiasis". The lesion responds to symptomatic treatment with the anti-histamine group of drugs. *L. E. Napier*

PAUTRIZEL, R. & MAYER, G. Les manifestations cutanées provoquées chez le cobaye par injections intradermiques d'extraits vermineux. [**Cutaneous Manifestations in the Guineapig caused by Intradermal Injections of Worm Extracts.**] *C. R. Soc. Biol.* 1948, Dec., v. 142, Nos. 23/24, 1551–2.

The following is a translation of the authors' summary :—

Intradermal injection of clean guineapigs with fractionated ascarid extracts provokes an intense leucocytosis involving all varieties of white cells. Similar injections made on guineapigs previously sensitized with the same extracts result in a considerable eosinophile infiltration, together with modifications of collagen fibres. These eosinophile infiltrations do not appear after intradermal injections of cestode extracts are made on animals sensitized with nematode extracts. *H. J. O'D. Burke-Gaffney*

PAUTRIZEL, R. & MAYER, G. Action d'un antihistaminique de synthèse sur les manifestations cutanées chez le cobaye par l'injection intradermique d'extraits ascaridiens. [**Action of a Synthetic Anti-Histamine Substance on the Cutaneous Manifestations in the Guineapig caused by Intradermal Injections of Ascarid Extracts.**] *C. R. Soc. Biol.* 1948, Dec., v. 142, Nos. 23/24, 1552–3.

The following is a translation of the authors' summary :—

The synthetic anti-histamine substance 3277 R.P. decreases the intensity of the cutaneous manifestations provoked by intradermal injection of ascarid extracts in guineapigs sensitized to these extracts : in particular, the amount and extent of the leucocytic infiltration are reduced.

H. J. O'D. Burke-Gaffney

PAUTRIZEL, R. & BAILENGER, J. Recherches sur l'hémotoxine ascaridienne. [**Studies on the Haemotoxin of** *Ascaris*.] *C. R. Soc. Biol.* 1948, Dec., v. 142, Nos. 23/24, 1550.

Different explanations have been put forward for the appearance of anaemia in helminthic diseases, a common one being that the worms secrete a haemotoxin : but not all authors accept this explanation.

FISHBACK [this *Bulletin*, 1931, v. 28, 225] reported the isolation from *Ascaris lumbricoides*, dried in a current of hot air, of a complex which was haemolytic *in vitro*. The present author asks whether this haemolytic complex was not in fact derived from bacteria present in the digestive tube of the worm.

He found that when an aqueous extract of *Ascaris* freshly prepared and stored at 4°C. or an aseptically taken specimen of coelomic fluid was added to a red-cell suspension, no haemolysis was observed : on the other hand, the aqueous extract, left at 37°C. for 24 hours was able to produce haemolysis. This seemed to suggest that the haemolytic property was related to the development of bacteria.

To test this hypothesis, he isolated bacteria from the digestive tube of *Ascaris* and maintained them on agar : these organisms were members of the *Proteus* group. A freshly prepared aqueous extract was sterilized at 120°C. for 15 minutes : this extract had no haemolytic action, even when left at 37°C. for several weeks. On the other hand, haemolytic properties appeared within a few hours if the extract was seeded with the *Proteus* isolated from the *Ascaris* itself and incubated at 37°C.

The author concludes that the haemolytic properties identified in extracts of *Ascaris* by different workers appear to be due to the presence of organisms of the *Proteus* group which are natural contaminants of the extracts.

H. J. O'D. Burke-Gaffney

KENNEY, M. & HEWITT, R. **Treatment of Bancroftian Filariasis with Hetrazan in British Guiana.** *Amer. J. Trop. Med.* 1949, Jan., v. 29, No. 1, 89–114. [21 refs.]

The results of trials with Hetrazan against Bancroftian filariasis in patients from British Guiana justify some degree of optimism. However, in very few cases recurrence of symptoms existing previous to treatment four months after cessation suggests that some adult worms have survived. Reduction in numbers of microfilariae of *W. bancrofti* is invariable with Hetrazan, but the degree of the initial microfilaraemia and the amount of drug within the range of 0·5 to 2·0 mgm. per kgm. are of little significance in this reduction. High initial counts (above 100 microfilariae per 60 cmm.) are less likely to show a reduction of 100 per cent. on the second day of treatment, but this varies in individuals. Few patients showed any microfilariae after one week of treatment, and the microfilarial counts remained negative, or at low levels, as long as follow-up examinations were made (up to 4 months after cessation).

It is believed that the effect of Hetrazan against the microfilariae of *W. bancrofti* is direct, since it occurs so rapidly. The systemic reactions which are presumed to be caused by the death of adult worms frequently do not occur until treatment has progressed for one or more weeks and the microfilariae have been cleared from the peripheral blood. No theories can at present be advanced regarding the mode of action of Hetrazan against microfilariae as it is practically ineffective in low dilutions *in vitro* against microfilariae of *L. carinii* and *D. immitis*, but does produce an observable *in vitro* effect on the microfilariae of *Folyella dolichoptera*. Several puzzling features have been recorded regarding the specificity of Hetrazan for various types of human microfilariae *in vivo*. It is effective against the microfilariae of *O. volvulus* and *L. loa* in the same doses as for *W. bancrofti*, but it is not effective against *A. perstans*, or *M. ozzardi* in the same doses, though higher doses might be so. If no other effect were produced other than that of rapidly reducing microfilariae in the blood the potential usefulness of such an effect in the control of filarial transmission in endemic areas is obvious.

It is known that Hetrazan has low toxicity in laboratory animals and that comparatively enormous doses are required to produce any evidence of damage. It is rapidly absorbed and excreted rapidly and exhibits no known cumulative effects. In therapeutic doses in man few side reactions have been observed.

Six volunteers, with no worm infections, took single doses of from 6 to 10 mgm. per kilo and had headaches, nausea, vomiting, malaise, apprehension and lassitude.

The occurrence of pains in various parts of the body, temporary swellings, localized rashes, nodular swellings and the temporary aggravation of pre-treatment swellings during Hetrazan treatment suggest that many of the adult worms were killed. It will be remembered that similar reactions were noted in untreated filarial cases in the S. Pacific area during the recent war and dead adult worms were removed from the sites of nodular swellings [this *Bulletin*, 1944, v. 41, 956; 1946, 43, 353].

The site of nodular swellings, lymphangitis, adenitis, urticaria, and accompanying symptoms which occur during treatment with Hetrazan may denote the position of the adult worms within the lymphatics. A parallel has been observed that in non-treated cases the exacerbation of symptoms coupled

with the disappearance of microfilariae is brought about by the death of the adult worms. The relative innocuous systemic reactions during treatment with asymptomatic reactions, regardless of the initial degree of microfilaraemia, suggest that these cases were considerably less sensitized to filarial protein than were the remaining groups of cases with histories of clinical symptoms at the time treatment was begun. The fever which occurred in these patients is probably related to the destruction of microfilariae. Polyuria which occurs in both asymptomatic and clinical groups is probably due to a true diuretic action of the drug.

Cutaneous manifestations seemed to respond to anti-histamine treatment with benadryl and ephedrine. The most dramatic and unexpected result of Hetrazan treatment was the partial recession or complete disappearance of pre-treatment swellings in a large proportion of cases. These ranged from partial diminution of swellings and softening of indurated parts to complete recession of swollen glands, swollen arms or legs, swollen spermatic cords and hydroceles, at varying periods during the course of treatment or after it had ceased.

The improvement in advanced cases of elephantiasis after treatment with Hetrazan may invite a complete revision of some of the contemporary conceptions of its pathology.

It is believed by some that the swelling in elephantiasis is due to the obstruction of lymphatics by dead or living filariae, sometimes complicated by secondary streptococcal infections. It is suggested from the effects produced by Hetrazan that the swelling is due, in some cases at least, to the presence of live worms which slowly release a foreign protein and produce allergic reactions resulting in chronic inflammation and oedema.

A part or all of the swelling is reversible after the source of inflammation is removed, even in old chronic cases. The time for the recession differs in different individuals, occurring in two weeks in some and several months after treatment in others.

Symptoms recurring in patients after cessation of treatment have been infrequent so far.

Eight patients have exhibited definite filarial attacks from 16 days to 2 months after treatment was stopped, and in 2 cases swellings recurred after they had been reduced by treatment. It is apparent that in these cases all adult worms had not been killed.

Recurring febrile attacks, subcutaneous nodules and generalized body pains were probably all of filarial origin and responded quickly to treatment with Hetrazan and complete relief was obtained.

During treatment many developed swellings in parts of the body where they had hitherto not existed, but with the exception of two these disappeared completely during the course of treatment. It was suggested that pre-treatment sensitization to filarial protein was intensified by a further increased amount of the same protein. These flare-ups subsided quickly.

These general conclusions are based upon a study of 296 cases of Bancroftian filariasis treated with Hetrazan in British Guiana. Rapid reductions of microfilariae were obtained when oral doses of 0·2 to 2·0 mgm. per kgm. of Hetrazan were given three times daily. Most cases treated with 0·4 mgm. per kgm. or higher showed negative counts one week after treatment had started. With a dosage of 0·2 mgm. per kgm. three times daily for three weeks or longer microfilariae may recur in small numbers at varying times after treatment has been stopped.

Atypical clinical manifestations of filariasis, simulating malaria, arthritis, or cutaneous diseases may be encountered in hyperendemic regions. These frequently respond to Hetrazan treatment. *P. Manson-Bahr*

Mazzotti, L. Posibilidad de utilizar como medio diagnostico auxiliar en la oncocercosis, las reacciones alergicas consecutivas a la administración del "Hetrazan". [**Allergic Signs after Hetrazan as a Subsidiary Diagnostic Measure in Onchocerciasis.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1948, Sept., v. 9, No. 3, 235–7.

In some patients infested with *Onchocerca* cutaneous biopsy is negative in result and nodules may not be present for examination, having been already extirpated. Skin reactions and complement fixation tests may give false positives, if the subject harbours other nematodes.

The author has observed that administration of Hetrazan (1 diethylcarbamyl 4 methyl piperazine) to patients harbouring *Onchocerca* gives rise to allergic phenomena in a few hours—cutaneous oedema and erythema-like erysipelatous patches ; if the eyes are involved they are almost closed by swelling of the lids, there is conjunctival congestion, axillary and inguinal adenitis, pains in muscles and joints and a rise of temperature to 39°C. The degree of reaction apparently varies with the degree of infection. These reactions were seen in 59 out of 65 patients and they faded within 5 days. These results were not seen when the drug was tried on patients with hookworm, *Ascaris*, *Enterobius*, *Trichuris*, *Strongyloides* or *Microfilaria ozzardi*, but *W. bancrofti* gives a similar reaction. The author concludes that in the absence of this last infestation, if allergic symptoms follow the administration of a single dose of 4 mgm. per kilo body weight, this is a valuable sign of infestation by *Onchocerca*.

H. Harold Scott

de Wit, J. C. De doelmatigheid van de behandeling van actieve oxyuriasis met vermifuga in de practijk. [**The Practical Value of treating Active Oxyuriasis with Vermifuges.**] *Nederl. Tijdschr. v. Geneesk.* 1949, Apr. 16, v. 93 (ii) No. 16, 1234–40. [21 refs.]

The English summary appended to the paper is as follows :—

" The author has treated two groups of 25 adults and two groups of 40 children suffering from active oxyuriasis, with gentian violet and phenothiazin respectively, two cures [courses] with a three weeks' interval, followed by control during one year. It appeared that phenothiazin is considerably more effective as a vermifuge than gentian violet, so that fewer relapses take place. The chances of reinfection, however, are so great that after a year 95 per cent of the patients in the gentian violet as well as in the phenothiazin groups were positive again, the number of patients without complaints then amounting to 30 per cent in both groups just as the number of worm carriers without complaints.

" Taking into account that phenothiazin in a dosage of 50 mg per kg body weight still gives light toxic symptoms, it seems indicated to reserve this medicament for very serious cases of active oxyuriasis, where quick results have to be obtained. However, the results are not permanent ; the solution of the oxyuris problem has to be sought in hygienic rather than in pharmacologic measures."

Larsh, J. E., Jr. & Hendricks, J. R. **The Probable Explanation for the Difference in the Localization of Adult *Trichinella spiralis* in Young and Old Mice.** *J. Parasitology.* 1949, Feb., v. 35, No. 1, 101–6. [10 refs.]

" Studies are described showing a distinct difference in the localization of adult *Trichinella spiralis* in young and old mice. In young mice significantly greater numbers were found in the posterior one-half of the small intestine

(average : 69·5 per cent), while the reverse was true in old mice (average : 18·7 per cent). Therefore, age apparently is a factor involved in this localization. Approximately the same percentage development of adult worms was found in mice of both age groups, showing no evidence of age resistance.

" In an attempt to demonstrate the mechanism of this difference in distribution, a study was made of the role of intestinal emptying time which is known to differ considerably in young and old mice. A reversal in distribution was shown in young mice by artificially decreasing their intestinal emptying time with morphine sulphate. In this case approximately 95 per cent of the worms were located in the anterior one-half of the small intestine. Although a direct comparison with old mice was not made, these results would seem to indicate that the difference in localization of the adult worms in mice of the two age groups is due chiefly to the difference in intestinal emptying time."

RIEDEL, B. B. **Milk as a Source of some Protection against the Acquisition of *Trichinella spiralis* in Mice.** *J. Parasitology.* 1949, Feb., v. 35, No. 1, 27–30.

" The effect of milk upon resistance of mice toward *Trichinella spiralis* was studied. On the sixth day after parasitism with 100± 8 cysts the average numbers of adult parasites harbored indicated that mice fed a commercial ration supplemented with whole milk harbored about the same numbers of adult parasites as mice fed the same ration supplemented with water. The smaller average numbers of larvae harbored 28 days after infection showed that whole milk supplementing a commercial, rat ration prevented many of the larvae from entering the general musculature of the mice."

GURSCH, O. F. **Intestinal Phase of *Trichinella spiralis* (Owen, 1835) Railliet, 1895.** *J. Parasitology.* 1949, Feb., v. 35, No. 1, 19–26, 2 figs. & 2 pls. [15 refs.]

" The results of these experiments demonstrated that in general the greatest percentage of recovery of *Trichinella spiralis* was from the first quarter section of the small intestine, and that the percentage of worms recovered from the following sections declined steadily.

" The larvae penetrated the mucosa immediately after ingestion. After 22 and 24 hours of infection, the worms were found again in the lumen. Subsequently, females as well as males penetrated the mucosa and caused extensive destruction of villi.

" After two days of infection, the adults recovered revealed a ratio of two females to one male. Even among those which were eliminated, that is, found in the cecum and large intestine, there were always more females than males".

LARSH, J. E., Jr. & KENT, D. E. **The Effect of Alcohol on Natural and Acquired Immunity of Mice to Infection with *Trichinella spiralis*.** *J. Parasitology.* 1949, Feb., v. 35, No. 1, 45–53.

DEFICIENCY DISEASES

BASSI, G. **Some Aspects of Glossitis caused by Vitamin Deficiency.** *Internat. Ztschr. f. Vitaminf.* Berne, 1949, v. 20, No. 4, 444–7, 4 coloured figs. on 2 pls.

" Glossitis is an important and early sign of vitamin deficiency, pointing to several causes. The least frequent is exogenic deficiency (insufficient intake of

the vitamin), which is practically never observed in Europeans, as is shown by the examination of prisoners and internees from German camps. More frequently it is caused by an imbalance in intermediatry metabolism in certain pathological conditions caused by, for example, diseases of the intestine and the liver, etc. Of great importance is deficiency caused by cellular inability to utilise the vitamin, through constitutional imperfections, particularly in people with hereditary tendencies (sons of syphilitics or alcoholics or mongoloid and negroid types) and in patients with a tendency to splitting of the junction tissues. In all these, there enters a factor that is neither exogenic nor intermediatry, but is linked with the peripheral cells ('disgenital inbalance ')."

VILTER, R. W., MUELLER, J. F. & BEAN, W. B. **The Therapeutic Effect of Tryptophane in Human Pellagra.** *J. Lab. & Clin. Med.* 1949, Mar., v. 34, No. 3, 409–13. [13 refs.]

" Tryptophane in 6 Gm. oral doses induced a remission in typical acute pellagrous lesions.

" It caused an increased excretion of N^1-methylnicotinamide in the urine of pellagrins at a slower rate but in the same manner as in normal persons.

" These observations suggest that tryptophane and niacin are closely related in their role in human as well as in animal nutrition."

SPRUE

STEFANINI, M. **Clinical Features and Pathogenesis of Tropical Sprue. Observations on a Series of Cases among Indian Prisoners of War in India.** *Medicine.* 1948, Dec., v. 27, No. 4, 379–427, 4 figs. [123 refs.]

Between March and June 1942, 12,500 Italian prisoners of war were transferred from various stations in India to a camp in Yol-Kangra Valley, where they remained until the beginning of 1946. This camp was situated at 4,000 feet in the Himalayan foothills where the humidity was high, especially during the rainy season, but the winter season, from December to February, was usually cold and rainy, followed by two months of dry weather.

The water supply was classified as oligomineral, not containing mica or silicon in excess.

After one year's residence in the area a large number of Italians developed goitre of the parenchymatous type and the number increased progressively even after salt fortified with iodine was obtained. Bacillary dysentery, benign tertian malaria, renal calculosis and acute appendicitis were the most common causes of admission to hospital. Surveys of the nutritional status were carried out every six months. The chief complaint was slight continuous loss of weight, though no signs of starvation nor of specific deficiencies were observed. Haematological data from 100 persons at random revealed a mild normocytic anaemia.

The first cases of tropical sprue were diagnosed in September 1942 and from then until the end of April 1945 a total of 1,069 cases of varying severity were encountered. Of these 268 were admitted to hospital. The length of time that the prisoners were resident in the area bore a direct relationship to the number of new cases ; furthermore, the incidence was clearly related to the atmospheric conditions for most of the cases occurred during and after the rainy season. The prisoners aged from 25 to 35 years showed a relatively greater number of new cases and relapses. The more serious cases were found in the oldest age

group, in which 80 per cent. of the patients who died were between 50 and 55 years of age.

One or more relapses, usually during or immediately after the rainy season were observed in 134 cases (12 per cent.). Death occurred in five, from aplastic anaemia. The past history was not helpful: 6 per cent. had suffered from bacillary dysentery during the year preceding the onset and 0·7 per cent. had chronic amoebic dysentery.

The recent history was rather uniform. Patients usually reported to hospital complaining of severe, uncontrollable diarrhoea, accompanied by distressing meteorism. Other symptoms were sudden severe asthenia, extreme irritability, nervousness and tenesmus. Many experienced difficulty in feeding themselves because of dysphagia.

The first stage of the disease is characterized by fatty diarrhoea and other early signs of intestinal malabsorption: the second is a multiple deficiency picture, while the third is a complex deficiency syndrome dominated by a hyperchromic anaemia typical of the full-blown picture of tropical sprue.

Among the symptoms of deficiency noted in the second stage, glossitis was present in 90 per cent.; small aphthae were observed; angular stomatitis with or without cheilosis was recorded in 27; and proctoscopic examination of patients complaining of tenesmus revealed a reddened and congested rectal mucosa. Several patients exhibited exfoliative dermatitis limited to the scrotum, thighs, abdomen, buttocks and dorsal surfaces of hands.

Studies of the haematological picture of 153 patients in the third stage revealed a hyperchromic macrocytic type of anaemia. The other results were as follows:—

Mean corpuscular haemoglobin, $\gamma\gamma$	33·8	(20·04)
Mean corpuscular volume, $c\mu$	123·34	(94·06)
Volume index (84)	1·47	(1·02)
Mean corpuscular haemoglobin concentration, per cent. ...	31·5	(37·9)
Saturation index	0·92	(1·15)

The values in brackets are calculated from the results obtained in 100 normal persons.

Sternal bone marrow biopsies were performed in 25 cases. With the exception of three, all showed typical erythroblastic arrest indistinguishable from that found in pernicious anaemia.

The serum calcium levels were always below normal, while the serum phosphorus values were within normal limits. Fasting blood sugar levels were consistently lower than normal.

The results of gastric analysis obtained in 97 cases showed mostly hypochlorhydria; there were six with histamine-responsive achlorhydria, and two with hyperchlorhydria.

Fat absorption and distribution of faecal fat were studied with difficulty in twenty cases. The average daily weight of stools was much higher than normal. The fat content was also increased, especially the third stage, but the ratio of split to unsplit fat was not much higher than normal. Despite the slight acid reaction of the faeces it was found that the split fat fraction consisted of soaps.

The average results showed that under the experimental conditions normal subjects absorbed approximately 90 per cent. of dietary fat, whereas sprue patients absorbed only 66 per cent.

During the three-year period 112 suffered a relapse during or immediately after the rainy season; of these 23 relapsed each year at the same time.

Autopsies performed in five fatal cases did not furnish any essential information, and postmortem examinations probably do not reveal conditions bearing on the functional derangements underlying the clinical symptoms.

Prognosis was favourable, especially when treatment was started early. A large number of cases have been followed since their repatriation to Italy and none has presented any further sign of activity of the syndrome.

Diet and rest formed the basis of treatment. Diet 1, high in animal proteins with protein/fat/carbohydrate ratio (P/F/C) of 1·0/0·23/0·95, was given to patients newly admitted to hospital with severe acute symptoms of the disease. Diet 2, which had a P/F/C ratio of 1·0/0·31/1·48, followed and continued till regression of active symptoms. Diet 3, with P/F/C ratio of 1·0/0·78/2·57, was given to all convalescent patients until clinical recovery appeared complete.

Fatty diarrhoea responded to diet alone. Sulphaguanidine was given to 175 patients in a dose of 4 gm. initially, 2 gm. every three hours on the first day and 1 gm. every three hours on the three following days, and resulted in arrest of the diarrhoea, and a feeling of well-being. Probably the action of the drug consists in suppressing the secondary infections which may be responsible for the severity of the diarrhoea.

Response to liver therapy was satisfactory, but less so in the third stage of the disease. Relief from diarrhoea and meteorism was obtained in from 7 to 10 days. Seventeen out of 153 patients did not respond to parenteral liver therapy. This number includes five who developed aplastic anaemia and the four who became chronic. The remaining eight cases who had severe macrocytic anaemia showed only a moderate reticulocyte response until they received transfusions or intramuscular injections of small quantities of blood. Full-scale therapy had practically no effect in the 4 chronic cases. The dietary observations confirm the fact that a high protein, low fat diet causes diminution in steatorrhoea, probably on account of the lower fat intake, so that with diminution of the irritant of fatty material in the intestine, diminution of the diarrhoea follows. The impression was confirmed that liver and yeast extract are highly effective.

Behaviour of oedema during treatment presented interesting features. In 43 cases occurrence of reticulocyte response and improvement of the haematological conditions were accompanied by an extension of the oedema. Later it regressed with concomitant marked increase of diuresis till it finally disappeared completely in 25 to 30 days. It was found that extension of the oedema, not associated with albuminuria or hypertension, was accompanied by a greater temporary fall of total serum proteins. This was possibly due to a greater demand of plastic material for active erythropoiesis. Relationship between hypoproteinaemia and extension of oedema under liver therapy was demonstrated by prompt regression of oedema after plasma transfusions.

The discussion of the results follows on familiar lines and reviews all the recent war-time literature on tropical sprue and allied syndromes, but does not lend itself to abstraction. It is concluded that dietary deficiency is known to be an important factor in the development of tropical sprue, but it cannot be considered the only cause of the disease, inasmuch as some peculiarities described in India during the war, as for instance the epidemic of sprue in a particular season of the year or its sudden high incidence in military units shortly after their transfer to certain areas could not be explained on the basis of " dietary deficiency " alone. Local, climatic and seasonal factors are therefore important in the pathogenesis of tropical sprue. *P. Manson-Bahr*

ZUCKERMAN, J. L., ZYMARIS, M. C. & NATELSON, S. **A Simple Method for the determination of Fecal Fat and Fatty Acids.** *J. Lab. & Clin. Med.* 1949, Feb., v. 34, No. 2, 282–6.

The method presented yields a result in 2½ hours after the stool is dry and 40 routine determinations may be performed in a working day.

The procedure is as follows : The stool is homogenized and a sample of about 2 gm. is dried at 60°C. overnight. The dried material is pulverized and to a weighed sample (500 mgm.) in a test tube with ground glass stopper are added 5 ml. of N-HCl, 5 ml. of a mixture of petroleum ether and ether (1 : 1) and 1 drop of 95 per cent. ethyl alcohol. The tube is stoppered and shaken for 25 minutes and then centrifuged for 15 minutes at 2,500 revolutions per minute. The ether mixture layer is aspirated into a weighed beaker, and the extraction process is repeated with 5 ml. of ether mixture. The solvent is evaporated on a steam bath, and the fatty residue is weighed. If free fatty acid determinations are required, the extracted fat is dissolved in 10 ml. of ethyl alcohol and titrated with 0·1 N-NaOH. *J. H. Birkinshaw*

Heyeraas, H. Deficit av folic acid og K-vitamin ved symptomatisk sprue. [**Deficiency of Folic Acid and Vitamin K in Symptomatic Sprue.**] *Nordisk Med.* 1949, Mar. 4, v. 41, No. 9, 420–21. English summary.

Report of a case.

Bie, K. Ileus hos spruepasient. [**Ileus in a Sprue Patient.**] *Nordisk Med.* 1949, Mar. 4, v. 41, No. 9, 418–19, 2 figs. English summary.

Report of a case.

Suarez, R. M., Hernandez-Morales, F., Marchand, E. J., Perez Santiago, E. & Torregrosa, M. V. **The Effect of Pteroyldiglutamic Acid (Diopterin) in Sprue.** *Bol. Asoc. Med. de Puerto Rico.* 1948, Oct., v. 40, No. 10, 282–7.

Diopterin is pteroyldiglutamic acid, which has been found to be only slightly active when assayed with *Lactobacillus casei* and *Streptococcus faecalis*. The relative potential amount of free folic acid in Diopterin is approximately 77 per cent.

The drug was given to six patients suffering from sprue either in the typical acute, or chronic stage in relapse, in doses of 50 to 200 mgm. daily. All six patients responded clinically and haematologically to the conjugate. The sternal marrow also showed the change from a megaloblastic or erythroblastic arrest to a normoblastic stimulation, similar to that observed with folic acid or with parenteral liver extract. An interesting observation was the presence of moderate or marked oedema of the legs during treatment and while the patient was showing definite improvement. This may be related to changes in the plasma proteins.

It appears from this small series that the daily oral administration of 50 mgm. of Diopterin is probably an adequate dose in the treatment of sprue, especially when given together with a full sprue diet. A capsule of 50 mgm. of Diopterin is equivalent to 37·5 mgm. of free folic acid. *P. Manson-Bahr*

HAEMATOLOGY

Macfarlane, R. G., King, E. J., Wootton, I. D. P. & Gilchrist, M. **Determination of Haemoglobin III. Reliability of Clinical and other Methods.** *Lancet.* 1948, Feb. 21, 282–6, 1 fig. [13 refs.]

The authors have attempted to estimate the degree of reliability of various methods of estimating haemoglobin. The factors that cause the variability in the results are discussed and the experiments were designed so that the effect of

each could be estimated separately, but in this paper they only deal with the total effect. Estimation of the iron content is generally accepted as the most reliable method of estimating haemoglobin and this has been used for judging the reliability of the various methods.

Eight large samples of " normal " blood were taken and divided between 16 representative observers in Oxford and 3 in London. Each of the Oxford workers estimated haemoglobin by 16 different methods, in 8 of which proprietary apparatuses were used, and 8 were experimental methods. The instruments used were the Haldane-Gowers, Gowers, Sahli (Hellige), Tallquist, Tintometer, Dare 1, Dare 2 and Sahli-Zeiss, and for the experimental methods the wedge colorimeter and the grey wedge photometer. With the two latter, 5 different haemoglobin derivatives were used for estimation, carboxyhaemoglobin, cyanmethaemoglobin and alkaline haematin, by both instruments, and acid haematin and oxyhaemoglobin, each by one instrument. Each member of the London group estimated the haemoglobin by 5 different instruments, Duboscq colorimeter, Duboscq photometer, straight grey wedges, circular grey wedge, and Sahli-Zeiss : in the case of the first four instruments, 5 different haemoglobin derivatives were used.

The results indicate that the dilution methods (Haldane, Gowers, Sahli) are the least satisfactory : differences of 10 per cent. or more must be registered before they can be regarded as significant. Whole blood methods are slightly better than the dilution methods. The simple Tallquist is little worse than the elaborate and expensive Dare 1 ; Dare 2 is slightly better. The Sahli-Zeiss is the best of the proprietary instruments.

Of the experimental methods the photometric are better than the colorimetric. The neutral grey photometer with either oxyhaemoglobin or alkaline haematin gave the best results in Oxford, but in London good results were obtained by the Duboscq photometer with all the haemoglobin derivatives and by the straight grey wedge with alkaline haematin and carboxyhaemoglobin. With these combinations, differences of less than 5 per cent. became significant.

L. E. Napier

King, E. J., Gilchrist, M., Wootton, I. D. P., O'Brien, J. R. P., Jope, H. M., Quelch, P. E., Peterson, J. M., Strangeways, D. H. & Ramsay, W. N. M. **Determination of Haemoglobin. IV. A Comparison of Methods for determining Iron Content and Oxygen Capacity of Blood.** *Lancet.* 1948, Mar. 27, 478–83. [22 refs.]

The best method of estimating haemoglobin in a sample of blood has been a subject of investigation for many years. The iron-content and the oxygen-capacity methods have been those most frequently used. The accuracy and relationship of these methods has been investigated in London, Oxford, Edinburgh and Cardiff by a number of analysts. Pigs', cows', and human blood were used in these trials. The iron content was determined by the titanous chloride method, and also by potassium bichromate titration and by an 8-hydroxyquinoline semi-micrograviметric method. The oxygen capacities were estimated by the Van- Slyke apparatus and by the Warburg apparatus. The " total haemoglobin " was also estimated after reduction with titanous citrate. Both saponin and a synthetic detergent were used for laking the blood. The carbon-monoxide capacities were also estimated, in Oxford.

" Excellent agreement was found on the same specimens among three different teams of analysts who used variations of the titanous chloride titration method for estimating blood-iron. A potassium dichromate iron-titration technique and a hydroxyquinoline micrograviметric iron method agree well with the titanous chloride procedure.

"Van Slyke oxygen-capacity results, obtained by three different analysts, agreed and were on an average 3·5% or 0·7 ml. of O_2 per 100 ml. of normal pig blood lower than the oxygen capacity calculated from iron analysis. For human blood the difference averages 2·0% or 0·4 ml. of O_2.

"An average difference of 1·1% or 0·23 ml. of O_2 was found between Van Slyke oxygen capacity and Ramsay's 'total haemoglobin' method on 14 pig bloods." The discrepancy between the iron and the oxygen methods is thus not entirely due to methaemoglobin which is included in this method.

"The Warburg apparatus may be used to measure oxygen capacity. It is less accurate than the Van Slyke method.

"No advantage was found in the substitution of a synthetic detergent for saponin in oxygen-capacity estimations.

"The carbon-monoxide-combining capacities of 6 human and 3 pig bloods were determined before and after reduction with sodium hydrosulphite. Some of these showed a slight increase in carbon monoxide capacity after reduction; two specimens showed a pronounced difference."

The object of this estimation is to determine the total haemoglobin present, since most temporarily inactive forms are capable of regeneration; the iron-content method is therefore more suitable as the standard base-line for judging the accuracy of clinical methods of estimating haemoglobin. It has the added advantage that it is less subject to fluctuations than the oxygen-capacity methods. *L. E. Napier*

King, E. J., Wootton, I. D. P., Donaldson, R., Sisson, R. B. & Macfarlane, R. G. **Determination of Haemoglobin. VI. Test of the M.R.C. Grey-Wedge Photometer.** *Lancet.* 1948, Dec. 18, 971–4, 4 figs. [13 refs.]

The experiments reported were designed to test the accuracy of the commercially produced Medical Research Council grey-wedge photometer. The experiments were carried out at the Postgraduate Medical School of London, and at the National Physical Laboratory, Teddington. Two instruments were used and 12 observers took part in the experiments.

The photometer is described: its main feature is an annular grey wedge which is rotated until the light passing through it equalizes the light passing through the coloured fluid in a cell. A monochromatic light filter is fitted over the eyepiece to make this matching possible. It can be used with daylight or artificial light; in the latter case a specially designed lamp is fitted to the instrument.

The results are shown on a histogram, a figure, and a table. The histogram shows that at least 90 per cent. of the 120 observations with artificial light fall within ± 2 per cent. of the true value and that no individual error is greater than 4 per cent. With daylight the result is almost as good; three observations are 5 per cent. above the true value.

None of the eight observers who went through the whole experiment showed any pronounced bias in favour of higher or lower estimates than the true values.

The authors issue a warning that in clinical practice the errors are likely to be larger, since in this trial errors associated with the taking of peripheral blood were eliminated by the use of venous blood, and special care was taken in ensuring accurate pipetting and cleaning of the instruments. [See also this *Bulletin*, 1948, v. 45, 359, for previous reference to this series.]

L. E. Napier

Méd. Trop. Marseilles. 1948, Nov.–Dec., v. 8, No. 5, 707–12. Nomenclature des cellules sanguines. [**Nomenclature of Blood Cells.**]

A detailed nomenclature prepared by a Committee established by the French Minister of Public Health.

Nagaty, H. F. & Zanaty, A. F. **The Treatment of Polycythaemia Vera. A Record of One Case treated with *Ancylostoma* Infection.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Mar., v. 42, No. 5, 493–9.

A number of methods of treatment for polycythaemia vera have been used: none has been uniformly successful. Duvoir *et al.* [this *Bulletin*, 1940, v. 37, 596] tried treatment by inducing a hookworm infection; the present authors report a case in which this treatment was again tried.

The patient was 55 years of age and had apparently suffered from polycythaemia vera for 10 years: when seen by the authors he showed a typical clinical and blood picture of the condition. His stools showed a few *Heterophyes heterophyes*, ova only. Between 30th April, 1946 and 14th May, 1946, 650 larvae from a culture of *Ancylostoma duodenale* were applied in drops of fresh water to his hands, feet, abdomen and back, and the drops allowed to dry. (On 15th June, 1946, 200 ml. of blood was withdrawn by venesection to relieve symptoms.) On 23rd September, 1946 it was calculated from a stool egg-count that he had 32 adult ancyclostomes. There was a slight fall in the total red-cell count, from 8×10^6 to below 7×10^6, a moderate leucocytosis, the increase being due to eosinophils which had risen from 1 per cent. to 36 to 65 per cent. Three hundred more larvae were applied to the abdomen between November and December, and in February, 1947 the egg count indicated 87 adult worms. There was a further drop in the blood count which was now 6,100,000 per cmm. After two more applications of larvae of 250 each to the abdomen in February, there was a rise in the egg count which on 14th April, 1947 indicated the presence of 420 adult ancylostomes and a further drop in the blood count to 5,100,000 per cmm. with 85 per cent. haemoglobin on 8th June, 1947. The final count on 5th November, 1947 showed 5,000,000 red cells per cmm., 60 per cent. haemoglobin (originally 140 per cent.), 12,000 leucocytes per cmm. with 27 per cent. eosinophils. There was a corresponding relief of symptoms; the man looked and felt better; he had no headaches, giddiness, or palpitations; and he was more efficient at his work: but he was still unfit for prolonged work. *L. E. Napier*

Zimmerman, S. P & Dugger, S. **Pernicious Anemia in the Tropical Negro.** *Arch. Intern. Med.* 1948, Aug., v. 82, No. 2, 184–95, 2 charts. [Refs. in footnotes.]

"1. Ten cases of pernicious anemia in the tropical Negro are presented.

"2. No essential differences were brought out in the manifestations of the disease in Negroes and in other races.

"3. Pernicious anemia does occur in tropical natives, and further study and increased awareness will cause it to be more frequently recognized."

Lehmann, H. **Macrocytic Anaemia in Central Africans in relation to Ancylostomiasis and other Diseases.** *Lancet.* 1949, Jan. 15, 90–95, 4 figs. [14 refs.]

Forty-four cases of severe anaemia in Uganda were studied. The patients were all over the age of 12 years and their haemoglobin was below 7 gm. per 100 ml. Control examinations on 27 well-nourished Africans showed the blood

pictures of all to be within the limits accepted as normal in Europe and India. Six of the controls had sickle cells compared with seven of the 44 anaemic patients.

The cause of the anaemia in 32 was ankylostomiasis and there was iron deficiency; in six others, this infection was complicated by malaria or a bacterial infection; and in the remaining six the anaemia was due to malaria or bacterial infection and there was no iron deficiency.

The author claims that :—

"The macrocytes in Central African anaemia are reticulocytes and young cells in general, emitted by an efficiently functioning bone-marrow into a periphery where constant blood-loss occurs."

He calls these macrocytes "coctic" cells and points out the difference between them and the megalocytes of pernicious anaemia and "nutritional macrocytic anaemia of Wills"; the main differentiating features are a low M.C.H.C. and the absence of any associated megaloblastic hyperplasia in the bone marrow.

[It is difficult to follow the author's reasoning in the use of the word "coctic" (=fully mellowed), since this is just what these cells are not.]

The pattern of recovery from the anaemia is as follows: At first there is a sharp rise in reticulocytes which is accompanied by a rapid rise in haemoglobin; the M.C.H. and M.C.V. increase rapidly but the M.C.H.C. is stationary. At the fourth week the reticulocytes are still high and the haemoglobin is still rising; the M.C.V. decreases and the M.C.H.C. starts rising slowly, but the M.C.H. which has reached the normal level earlier remains stationary. At the end of eight weeks there is still a reticulocytosis (4–10 per cent.), the haemoglobin is still submaximal and the M.C.V. is still above normal. At this stage a return to normal values will only follow anthelmintic treatment.

"The removal of hookworms leads to darkening of the skin in patients whose iron deficiency has been corrected. It also causes the disappearance of other kwashiorkor symptoms. The possibility is discussed of inhibition by parasites of tyrosine oxidation being the cause of both the pale skin and, at least partially, the escape of coctic cells into the blood-stream. Tests in which tyrosine is injected into the skin are described to support the first part of this theory.

"It is emphasised that the extermination of parasites will have to be an essential measure in the prevention of kwashiorkor."

The author implies, though he does not actually state, that parasitization is more important than malnutrition in the production of kwashiorkor.

L. E. Napier

RAPER, A. B. **Sudden Death in Sickle Cell Disease.** *East African Med. J.* 1949, Jan., v. 26, No. 1, 14–22. [23 refs.]

While much has been written on the sickle-cell trait in America, until recently, little attention has been directed to it in Africa, and this has been mainly to the clinical aspects. The author reports the autopsies with clinical notes in five cases of sudden death, in which he considers that the sickling was the main cause of death.

(1) A child, aged 1½ years, had a short febrile illness and died suddenly. The vessels of the cerebral cortex and medulla were packed with sickle cells and in the medulla there was perivascular extravasation. There was no evidence of meningitis or poliomyelitis. Other organs had their vessels similarly packed with sickle cells and the spleen showed the typical sicklaemic lesions.

(2) A child of 8 years with a history of fever and pain in the chest for 5 days became comatose and died on the third day after admission to hospital. The brain cortex was a bright pink. Histological sections showed the vessels packed with sickle cells but no evidence of encephalitis or meningitis.

(3) A child of one year died after three days fever with diarrhoea and vomiting. The right lower lobe was consolidated but had an unusual appearance unlike that of red hepatization. The brain was not examined but other organs had their vessels packed with sickle cells. The vessels in the alveoli of the lung were similarly packed and there were only scanty polymorphonuclears and macrophages but no organisms in the consolidated parts. [The author considers that death occurred at too early a stage to be attributed to pneumonia alone.]

(4) A man, aged 23, died 20 minutes after admission. The brain showed extensive blocking of venules with sickle cells with rupture of the vascular wall and extravasation in places.

(5) A young woman, aged 16 years, died suddenly three hours after a forceps delivery with prolonged anaesthesia. Liver and kidney showed sickle cells distending the venules, and there were " sicklaemic haemorrhages " in the spleen.

The author points out that the well-known sickle-cell anaemia is only one result of the sickle-cell trait and that persons in whom the trait is well-developed are liable to medical accidents as the result of sudden extensive sickling of their cells. The precipitating fact he considers to be generalized anoxaemia from any cause, *e.g.* an acute infection, prolonged anaesthesia.

The author discusses the incidence of the sickling trait in Africa, especially in Uganda : he concludes that the incidence in and around Kampala is about 20 per cent. in children and 10 per cent. in adults. This discrepancy indicates that a large number of the children with the trait do not live to become adults.

L. E. Napier

DA SILVA, E. M. Verificações sôbre a incidência de siclemia em índios brasileiros. I. Indios Pariukur, Galiby, Caripuna, Canella e Carnijó. [**Study of the Incidence of Sicklaemia in Brazilian Indians.**] *Mem. Inst. Oswaldo Cruz.* 1948, Mar., v. 46, No. 1, 125–34. [10 refs.]

The English summary appended to the paper is as follows :—

" Research of sicklemia in 671 putatively full-blooded Brazilian Indians was negative. These Indians belong to seven different tribes.

" Among 166 individuals of Carnijó of Fulniô tribe 3 were sicklemic (sicklemia index 1·8%). This tribe is very mixed.

" In the table above these results are summarized :

" These observations show that sicklemia test is a useful tool in anthropological investigations."

TROPICAL OPHTHALMOLOGY

A Review of Recent Articles. LII*

Blindness.—An analysis of the causes of blindness in West China was made both aetiologically and topographically by Shen.[1] A total of 1,130 blind eyes in 748 patients was investigated. In this series of cases, trachoma is the principal cause of blindness in West China and was responsible for 438 blind eyes. Ulcerative keratitis from various causes occupies the next position and was responsible for blindness in 158 eyes. Keratomalacia is prevalent among the poor and was responsible for 90 blind eyes. The majority of the patients were children under 10 years of age. Only 6 patients were adults. Gonorrhoea is another important cause of blindness especially in infants, and was responsible for 100 eyes. Of these, 66 eyes occurred in adults.

Many babies are delivered by untrained midwives and Credé's prophylactic treatment is not carried out in most parts of China.

Syphilis was responsible for 43 blind eyes. Of these, one alone was due to congenital syphilis and the remainder to the acquired form.

Smallpox and hereditary defects are to-day uncommon causes of blindness in West China.

Trachoma.—The discovery of the trachoma agent is discussed in a paper by Taborisky.[2] This paper was sent by the authors to Budapest in 1931 in competition for the trachoma prize, and has not hitherto been published. The reason why he himself has not published this paper sooner is because his conclusions were based upon facts published in previous articles and he awaited their confirmation by other investigators and also that a single link was missing in the chain of proofs of the aetiological significance of Prowazek-Halberstaedter bodies (PHB), namely the culture of these bodies and their successful inoculation to man and monkey.

It has been admitted that the common bacteria met with in trachoma and the Noguchi bacillus are not of any aetiological significance. The author is of opinion that the elements of the inclusions, the initial bodies (i.b.) and the elementary bodies (e.b.) are the infectious agents of the disease. These are known as the Prowazek-Halberstaedter's bodies (PHB) and the elements of these are the virus of trachoma. They are also found in blennorrhoea neonatorum and bath conjunctivitis (inclusion conjunctivitis). The similarity of clinical symptoms and pathological peculiarities in trachoma, blennorrhoea neonatorum and bath conjunctivitis obviously indicates a near relationship of their agents. The difference between these three diseases, the author considers, is only one in virulence such as between variola and vaccinia. Blennorrhoea neonatorum and bath conjunctivitis are mild diseases without complications, clearing up even without treatment, while trachoma is a long and severe illness with frequent complications requiring prolonged treatment.

The particles of trachoma virus, the e.b., differ from the e.b. of psittacosis and lymphogranuloma in their size and mode of staining and particularly in their biological properties. Thus a specific organism is found in trachoma which is not to be found in other diseases, according to the first postulate of Henle-Koch. There remains the question whether the PHB are present in all or only in some of the cases of trachoma. The whole course of the disease offers conclusive signs of the close connexion between the inclusions and the clinical symptoms of trachoma. The presence and disappearance of the PHB depends

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*For the 51st of this Series see Vol. 45, pp. 1109–1112.

[1] Shen, D. S. Investigation of Blindness in West China. A Statistical Review. *Chinese Med. J.* Chengtu Edition. 1945, Jan., v. 63A, No. 2, 62–7. [11 refs.]

[2] Taborisky, J. The Discovery of the Trachoma Agent. *Acta Med. Orientalia.* 1948, Apr., v. 7, No. 4, 61–71, 2 figs. [Numerous refs.]

on (*a*) the time passed from the beginning of the disease, (*b*) the severity of the disease and (*c*) the treatment. In medium and severe cases the PHB are always found in the first months of the disease, in spite of every treatment. The inclusions disappear when the disease becomes regressive or remains stationary. If the virus becomes active again, the inclusions may reappear. As to the third postulate of Henle-Koch, namely the growth of elements of PHB in culture and their transmission to man and animals, no positive results have so far been obtained. [See MACCHIAVELLO, this *Bulletin*, 1948, v. 45, 1112].

The campaign against trachoma in Morocco is discussed by DELANOE[3]. He came to the conclusion that eye washes and ointments were of little use in treatment and he sought a remedy to attack the actual organism of the disease. He found that the granulations were identical with those found in tuberculosis and akin to those found in leprosy. He has employed local treatment by applying chaulmoogra oil to the granulations and found even after the first application that improvement was apparent within a week. Pain, photophobia, blepharospasm and inflammation all became less. In the course of time the granulations became smaller and ultimately disappeared.

The treatment is painless, easy to carry out and the cost is trivial.

The author published his first paper on the treatment of trachoma by local applications of chaulmoogra oil in 1925 [this *Bulletin*, 1926, v. 23, 920].

A statistical study of trachoma among in-patients is discussed by CHI[4] in Chengtu. Of 2,903 patients admitted to the Department of Ophthalmology of the Chengtu Eye, Ear, Nose and Throat Hospital from January 1940 to December 1943, 1,305 patients, *i.e.*, 44·9 per cent., were diagnosed as having trachoma. The sex ratio was 54·6 per cent. females to 45·4 per cent. males. The ages of the patients in 65·1 per cent. of cases ranged between 16 and 40 years of age. The majority of the patients had trachoma stage III (MacCallan) ; nearly all of the cases showed some sequelae and 31·9 per cent. were classified as blind on admission. The most important factor, as a cause of blindness in trachoma, was a lesion of the cornea and so to reduce the incidence of blindness it is essential to control the spread of trachoma.

CHAN[5] presents a set of figures on trachoma among the in-patients of the same hospital for the year 1938 to 1939. These figures are supplementary to those published by Chi and are analogous. He points out the high incidence of keratitis as well as trichiasis and entropion in trachoma stage III. He further calls attention to the frequent association of entropion or trichiasis with keratitis and that trichiasis or entropion are usually bilateral.

Leprosy.—Lagophthalmos in leprosy is discussed by CHATTERJEE and DHARMENDRA.[6] The condition is sometimes seen in leprosy and more frequently in the neural than in the lepromatous type and often leads to complications such as conjunctivitis, keratitis, corneal ulceration, leucoma, iritis, panophthalmitis and phthisis bulbi. The condition and its complications are well recognized but what is not always appreciated is that they are often preventable by timely treatment.

Lagophthalmos is caused primarily by paralysis of the orbicularis oculi and possibly the deformity is later exaggerated by the unopposed action of the levator pelpebrae superioris muscle. In more advanced cases the orbicularis oculi is completely atrophic and the eyelids are fully retracted.

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[3] DELANOE, E., Mme. Lutte contre le trachome au Maroc. *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 9/10, 627–8.

[4] CHI, Hsiu-hsiang. A Statistical Study of Trachoma among In-Patients. *Chinese Med. J.* Chengtu Edition. 1945, Jan., v. 63A, No. 2, 73–9. [16 refs.]

[5] CHAN, E. A Statistical Study of Trachoma among In-Patients. *Chinese Med. J.* Chengtu Edition. 1945, Jan., v. 63A, No. 2, 93–7.

[6] CHATTERJEE, S. N. & DHARMENDRA. Lagophthalmos in Leprosy. *Leprosy in India.* 1947, Apr., v. 19, No. 2, 44–8, 7 figs. on 4 pls.

It is usually associated with a leprous lesion on the affected side involving the eyelids and the adjoining skin. In a lepromatous case the lesion is in the form of a diffuse infiltration or nodulation and paralysis is sometimes noticed when the lesions subside : in a neural case the skin may be hypopigmented and flat or red and thick. It may be or may not be anaesthetic but sensation of pain on pin-prick is diminished in all cases.

Lagophthalmos may be present when the patient first attends for treatment or it may occur later during the course of treatment. Lesions on the face and eyelids do not always give rise to lagophthalmos. It may or may not be accompanied by loss of sensation of the conjunctiva and cornea, and the anaesthesia may be found before the lagophthalmos sets in. It is responsible to a certain extent for the associated conjunctivitis and keratitis, since it interferes with the natural defensive mechanism of the eye by allowing foreign irritating particles to remain unnoticed in the tissue. When lagophthalmos supervenes, the defensive mechanism is further interfered with and the result is constant irritation causing conjunctivitis, keratitis and ulceration of the cornea, which may lead to leucoma or panophthalmitis.

The treatment of lagophthalmos consists in prevention as well as cure. Unless there are present signs of reaction, all cases of leprosy with lesions in or around the eyelids should receive preventive treatment on the following lines :—

Injections of creosoted hydnocarpus oil should be given around the orbit including the eyelids. The injections are given by the intradermal method once in three weeks. In the interval, weekly injections of the oil are given in other lesions if there be any, or intramuscularly into the buttocks. The injections are continued until the lesion fades and there is partial return of sensation. When the conjunctiva and cornea are anaesthetic, the affected eye should be protected by using tinted goggles and liquid paraffin is frequently dropped into the conjunctival sac to counteract the effects of drying.

The curative treatment of lagophthalmos has to be on the same lines as the preventive treatment but has to be more vigorous. The hydnocarpus oil is better injected subcutaneously. About 1 cc. of the oil can be injected in the eyelids once in three weeks at one sitting. The treatment should be continued for some time after the correction of the defect, so that the results obtained may be maintained. Liquid paraffin should be dropped into the eyes frequently and if there be no ulceration the affected eye should be bandaged at night. If ulceration of the cornea occurs, it should be treated with atropine drops or ointment and a pad should be applied. When there is not much discharge, the affected muscles should be massaged daily for about half an hour and the patient should be instructed to move his eyelids frequently.

With this treatment lachrymation diminishes and there is a gradual return of power to the affected muscles within three months. In advanced cases the surgical treatment of lateral tarsorrhaphy or canthorrhaphy should be combined with medical measures.

A report of leprosy lesions of the fundus in a case of lepromatous leprosy of fifteen years duration is discussed by ELLIOTT.[7] The patient, a corpulent white male, 43 years of age, reported to the eye clinic complaining of sudden loss of vision in the left eye. He had been reading when he became aware of this difficulty and when seen two hours later had no other symptoms except slight discomfort. Upon examination there was slight circumcorneal injection. The pupils were active. The fundus presented an array of creamy white, waxy-surfaced, pedunculated "pearls", projecting from the retina and situated

[7] ELLIOTT, D. C. A Report of Leprosy Lesions of the Fundus. *Internat. J. Leprosy.* 1948, July–Sept., v. 16, No. 3, 347–50, 1 fig.

from one to two disc diameters from the optic disc. In all there were twelve such lesions and they were identical ophthalmoscopically with those seen on the iris in this patient and in others. Iris lesions of this kind have been histologically proven to be true lepromas and contain typical lepra cells, Hansen's bacilli and round-cell infiltrations. In this patient lepromata of the iris were present in each eye, but the retinal lesions were found only in the left eye. During observation, it was found that these iris and retinal lepromata were transient formations developing and receding within a period of eight months duration.

This was the only case of a retinal leprous lesion in the examination of over 500 fundi.

In an addendum the author states that since this article was written, three other cases of leprous lesions of the fundus of the eye have been demonstrated.

Vitamin B deficiency.—The article by DAWSON, FINDLAY & WARD [this *Bulletin*, 1949, v. 46, 278] on vitamin B complex deficiency states in West Africa is discussed by Fitzgerald MOORE.[8] He points out that the dietaries of the Gold Coast, Sierra Leone and Southern Nigeria differ markedly in the staple foodstuffs and, as would be expected, in the expression and symptomatology of deficiency disease. Again, only certain sections of the peoples show manifest evidence of these conditions and the severity of them is primarily determined by economic circumstances. Generally speaking, the Gold Coast is much less affected with frank nutritional disease than is either Sierra Leone or Southern Nigeria. Though kwashiorkor is more common in the Gold Coast, neither the very extensive dietary and clinical survey of PURCELL nor of Beatrice RUSSELL have recorded any real incidents of nutritional retrobulbar neuritis there, in great contrast to these other two colonies.

Nutritional retrobulbar neuritis (followed by partial optic atrophy) can occur independently of either beriberi or ariboflavinosis or along with these diseases, and the signs of these two latter will rapidly disappear with the return to a normal diet, but not so the central neuritic condition. In Southern Nigeria beriberi is a practically unknown, even recorded diseased. Ariboflavinosis was excessively common among the manioc eaters and associated with it, nutritional retrobulbar neuritis (in the active phase). Ariboflavinosis was, however, not seen among the yam eaters, who only used manioc as a secondary staple foodstuff. The degree of ariboflavinosis varied considerably, and in Nigeria was not as severe as among the rice-eating population of Sierra Leone. For example, frank keratitis was rarely seen in Nigeria, but was exceedingly common among the Sierra Leone sailormen and Kroo boys. The incidence of nutritional retrobulbar neuritis in relation to ariboflavinosis varied considerably. The highest rate found by the author was 12 per cent. By contrast, a high percentage of pregnant women attending the ante-natal clinic in Lagos showed ariboflavinosis, but it was rare to find nutritional retrobulbar neuritis.

H. H. SCOTT showed in the central neuritis of Jamaica that beriberi was not present in those cases. WRIGHT described the A and B avitaminosis of Sierra Leone and considered that the condition was apart from beriberi. Likewise, the work of STANNUS and many others does not support beriberi as a cause of retrobulbar neuritis. Thiamin was found of little value in nutritional retrobulbar neuritis in prisoners of war camps, both in its failure to cure and to prevent the condition. The author, in Nigeria, was successful with autoclaved marmite, which was as efficient as ordinary marmite, always provided the cases were seen early enough. The aetiology of nutritional retrobulbar neuritis both as regards the exact curative or preventative factor or factors is still not known. It is possible the cobalt-containing vitamin B_{12}, which according to

[8] MOORE, D. F. Vitamin B Deficiency States. [Correspondence.] *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Jan., v. 42, No. 4, 412–13.

Spies, possesses a powerful antineuritic effect, may provide the solution. It is also possible it may not be a vitamin at all, but that " something else " in marmite and yeast and still unidentified.

Thelaziasis.—Thelazia infestation of the conjunctival sac in China is reviewed by Liang.[9] He gives the history of four cases reported by others and describes a fifth case seen by him. All the cases were caused by *Thelazia callipaeda*. Animals infested with *Thelazia* are known to be widespread in China and the worm may involve the eyes of mammals and birds. Thelaziasis, as do other parasitic diseases, produces an eosinophilia in the blood. When present in the conjunctival sac it produces symptoms of foreign body irritation, intense pain and lachrymation and causes verminous conjunctivitis. The cornea may become cloudy as a result of irritation by the worms. Occasionally there may be no subjective symptoms in the infected eye, the parasites being discovered during the routine examination. *E. O'G. Kirwan*

HEAT STROKE AND ALLIED CONDITIONS

Mom, A. M. El empleo de la protección antisolar y de los repelentes de insectos en los indigenas latinoamericanos. [**The Use of Insect Repellents and Anti-sunburn Substances among the Latin-Americans.**] *Rev. Argentina de Dermatosifilologia*. 1948, July–Dec., v. 32, Nos. 3/4, 303–6. [35 refs.]

Hernandez is quoted as having mentioned, nearly 380 years ago, that the Mexican Indians used an aromatic resin, believed to have been *Liquidambar styraciflua*, as a protective ointment. Substances in later use have been obtained from *Bixa orellana* and having many synonyms according to locality (more than a dozen are mentioned) ; one of these is *urucú*, and the medical term for anointing the body with the red juice is *urucuization*.

An analysis of the seed of *Bixa orellana* by Chevreuil in 1833 showed it to contain a water-soluble yellowish colouring matter, *orellina*, and a red substance, *bixine*, soluble in oils. It is the latter which is used as an ointment with a fatty basis, either animal as capibara, iguana, or fish oil, or vegetable as palm oil. It is used as a protective from the sun's rays and also as a repellent of insects, especially mosquitoes. Being insoluble in water it is not affected by sweat. The women anoint the men with it before the latter go to work in the sun, or to hunt or fish, and " they return from fishing in a canoe with their backs covered with dead mosquitoes ". The seeds are also used medicinally as a laxative and as a condiment with rice.

The experiment was made of exposing three thermometers to the sun ; one had the bulb silvered, another was covered with *urucú*, the third had the bulb blackened. The first gave a reading of 32°C., the second 33°C., the third 40°C. *Urucú* therefore protects against the sun's action, both the heat and the actinic rays, but does not prevent the evaporation of sweat.

In drier and colder regions where *Bixa orellana* does not grow, or grows only with difficulty, infusions of the bark of certain trees of the *Simaruba*, *Simaba* and *Picrasina* genera are used as repellents. *H. Harold Scott*

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[9] Liang, S. C. Thelaziasis of the Conjunctiva. *Chinese Med. J.* Chengtu Edition. 1945, Jan., v. 63A, No. 2, 70–72.

VICK, F. Ueber den Wärmeschutz der Tropenzelte. [**Protection of Tents in the Tropics from Alterations in Temperature.**] *Acta Tropica*. Basle. 1949, v. 6, No. 1, 47–50, 4 figs.

Tents have the great merit that they are readily transportable, but they possess the serious disadvantages that when exposed to solar radiation they act as heat traps and become too hot, while by night they are too cold.

In this paper the author deals with the protection of tents in the tropics, and gives the results of observations made in North Africa, in Southern Italy, and in the Alps.

Of three single-walled tents, otherwise of similar type, one had no sun canopy, one had a normal canopy, and the other had a canopy lengthened to about 2½ metres. In the heat of the day the temperature in the tent without a canopy was about 11·4°C. above the external temperature, while in the tents with canopies the temperature excess was 3·4°C. to 4·6°C. The lengthened canopy was an advantage, for it kept the inside temperature lower than that in the tent with the normal canopy. A double-walled tent had a temperature about 3°C. above the outside temperature. It is an advantage to ventilate the space between the inner and outer walls, thus the tent is kept cooler. Ventilation of the tent has a substantial cooling effect. A graph shows that when the tent was closed the temperature within it was about 5°C. above that of the air outside. When the tent was then opened the temperature fell rapidly, so that after a few minutes the excess over the outside temperature was only about 1°C.

A canopy above the tent reduces radiation from the tent to the night sky, and thus affords some protection against excessive cooling.

The protection given by a canopy would be substantially increased if its surface were metallized, for radiation would thus be reduced.

Thomas Bedford

ENTOMOLOGY AND INSECTICIDES: GENERAL

DESCHIENS, R. & PICK, F. Le choix des surfaces de ponte par *Aëdes aegypti* (*Stegomyia fasciata*) dans des conditions expérimentales. [**Choice of Surfaces for Oviposition by *Aëdes aegypti* in Experimental Conditions.**] *Acta Tropica*. Basle. 1949, v. 6, No. 1, 1–12, 11 figs.

About 30–50 *Aëdes aegypti* females fed on a guineapig four to five days previously were provided at 27°C. with the choice of two or more moist substances on which to oviposit. The substances tested include silica-gel (SiO_3), a clay paste, kaolin paste (SiO_3/Al_2O_3), magnesium silicate paste, calcium carbonate paste, water, and filter paper moistened with water or with honey-sweetened water. Each substrate was placed in a separate Petri dish and after 24–120 hours the number of eggs in each dish was counted.

In preliminary tests 89·5 per cent. of 522 eggs were deposited in a dish of silica-gel and only 10·5 per cent. in clay paste. In subsequent experiments, the following percentages of 563 eggs were obtained on several different substances provided simultaneously: silica-gel (78·68 per cent.); clay paste (13·85 per cent.); honey-sweetened water (5·1 per cent.); water-moistened filter paper (2·3 per cent.) and in water alone (nil). Numerous experiments of this sort are detailed and the conclusion is made that silicaceous substances are particularly attractive to ovipositing females and that silica-gel is preferred rather than any of the other compositions tested.

Investigations were also made in the case of silica-gel and the clay paste on the effects of the physical nature of the surfaces on oviposition. In each case

the surface of the medium in the Petri dish was quartered. One sector was left smooth, another was striated radially, whilst the third was striated in concentric arcs, and the fourth quarter was roughened by punctations. The grooves of the striated parts were 1 mm. deep and 1 cm. apart.

Eggs were laid almost exclusively in the roughened sectors especially in those striated radially or in concentric arcs. The eggs were found in the furrows.

It is thought that the surface formation of the striated areas affects oviposition in virtue of changes in the humidity of the environment near or above the grooves.

The authors suggest that these results may be of use in breeding *Aëdes* in the laboratory or in providing attractive oviposition surfaces for "trapping" eggs from gravid females in nature. *D. S. Bertram*

Downs, W. G. & Baker, R. H. **Experiments in Crossing** *Aëdes* (*Stegomyia*) *aegypti* **Linnaeus and** *Aëdes* (*Stegomyia*) *albopictus* **Skuse.** *Science.* 1949, Feb. 25, 200–201.

A report on small scale experiments in crossing *Aëdes aegypti* and *Aëdes albopictus*, in which only a few non-viable eggs were obtained from *albopictus* ♀ x *aegypti* ♂ crosses, whereas *aegypti* ♀ x *albopictus* ♂ crosses resulted in fertile progeny bred to the second generation of adults. All the F_1 mosquitoes and those examined of the F_2 generation resembled *Aëdes aegypti* in every detail, including male genitalia and larval characters. Resemblance to the parent female has been observed by other authors in successful crosses of *albopictus* females and *aegypti* males. It is noted that these results are not easily explained on a genetic basis.

The original laboratory strains of *Aëdes aegypti* and of *Aëdes albopictus* available to the authors were not certainly pure stock. *D. S. Bertram*

Farid, M. A. **Relationships between certain Populations of** *Culex pipiens* **Linnaeus and** *Culex quinquefasciatus* **Say in the United States.** *Amer. J. Hyg.* 1949, Jan., v. 49, No. 1, 83–100, 2 figs.

In the United States *Culex pipiens* L. is a common domestic mosquito in the northern States. *Culex quinquefasciatus* Say (*fatigans* Wiedemann) replaces it in the extreme southern States and both species occur together in intermediate States, *e.g.* in North and South Carolina. The present paper is an account of a laboratory investigation into the factors controlling the distribution of these two species and deals also with the validity of their specific status.

Four mosquito populations were studied: *C. pipiens* from Michigan and from Baltimore; *C. quinquefasciatus* from Texas, and a laboratory colony referred to as *C. quinquefasciatus*, believed to have originated in Mississippi or Alabama, and having intermediate morphological characteristics between *C. pipiens and C. quinquefasciatus.*

At *low temperatures* (2–2·5°C. and 6–6·5°C.) aquatic stages of *C. pipiens* (from Michigan) and *C. quinquefasciatus* (from Alabama) showed no appreciable differences in their survival rates. More than eighteen hours at 2–2·5°C. and thirty-six hours at 6–6·5°C. prevented eggs from hatching. These were, however, recently laid eggs; eggs twenty-four hours old remained viable even after five to six days at 2–2·5°C. No larvae survived more than three days at 2–2·5°C. and only 3–4 per cent. of pupae survived five days at 6–6·5°C. At moderately low temperatures of 13·5–14°C., no marked differences were found in the duration of the aquatic stages. Thus, the eggs hatched in 5·9–6·3

days, the first, second, third and fourth stage larva required respectively 5·7–6·2 days, 4·3–4·4 days, 5·3 days, and 9·0 to 9·4 days. A slightly better survival rate for the *pipiens* larvae was not found to be statistically significant. [No observations for pupae are given at this temperature.] Emergence from pupae occurred at 16·1°C. in both species and, at this temperature, both species fed on pigeon within three days and laid fertile egg rafts nine to twelve days later. It is concluded that, at low temperatures, no appreciable differences were observed between these strains of *C. pipiens* and *C. quinquefasciatus* as regards survival and the rate of development of the aquatic stages nor in the feeding and mating habits of the adults.

Five-minute exposures of the aquatic stages of all four populations to *high temperatures* showed that the lethal temperatures for 50 per cent. kills varied only within the narrow ranges of 42·1 to 43·0°C. (for eggs), 41·3 to 42·3°C. (larval stages), and 42–42·1°C. (pupae). The duration of the various stages bred at high temperatures (31–34°C.) were as follows: 25–28 hours for the eggs, 1 day for each of the first three larval instars, 3–4 days for the fourth instar larva and 24 hours for the pupae. Eggs hatched at 33°C. but not at 34·5°C. There were no appreciable differences in the survival rates of these various stages and 16·5 per cent. of *C. pipiens* and 17·7 per cent. of *C. quinquefasciatus* matured to adults. Adult activity at 31·5°C.–32°C. and a relative humidity of 93 per cent. was studied for *C. pipiens* (Michigan), *C. quinquefasciatus* (Alabama) and the southern form of *quinquefasciatus* from Texas. Females of all three populations fed on pigeon but only the Texas form of *C. quinquefasciatus* produced seven completely fertile egg rafts, the other strains producing four out of five (*pipiens*) and seven out of eight (*quinquefasciatus*) infertile rafts. The fertility of the rafts increased, however, when both these strains, which still included males, were transferred to room temperatures [temperature not stated but, presumably, moderate] the conclusion being drawn that at the high temperature mating had not occurred with normal success. It is concluded that, apart from this indication that the Texas population of *C. quinquefasciatus* mates more readily than *C. quinquefasciatus* from Alabama and *C. pipiens*, no appreciable differences were observed at high temperatures between *C. pipiens* and *C. quinquefasciatus*.

All four populations paired on the wing, mated in 5 in.-cube cages, and were anautogenous, requiring blood meals for the production of fertile eggs.

Cross-matings between all four populations resulted in fertile progeny, and in the case of both types of pairing of *C. pipiens* (from Michigan) and *C. quinquefasciatus* (from Alabama), the hybrid stock was bred to the eggs of the F_3 generation. All other crosses were maintained as far as the eggs of the F_2 generation. Sterile rafts were rare.

The author gives reasons for suggesting that the absence of *C. quinquefasciatus* in the north is due to its inability to hibernate or to withstand more than about a hundred days of North Carolina winter conditions; possibly, a reluctance to mate at low temperatures also plays a part in limiting its northern distribution. Hibernation enables *C. pipiens* to survive the colder northern climate and its absence in the south may, it is suggested, be due to inability to mate satisfactorily at high temperatures.

It is observed that in nature transitional forms between *C. pipiens* L. and *C. quinquefasciatus* Say have been reported by many workers and, in view of this and of the results obtained in cross-breeding the four populations dealt with in the present study, it is suggested that the differences between the species are no more than infraspecific. The following nomenclature is, therefore, proposed: *C. pipiens pipiens* L. 1758 from Michigan and Baltimore; *C. pipiens quinquefasciatus* Say 1832 for the *C. quinquefasciatus* population from Texas; the *quinquefasciatus* population from Alabama occupying an

intermediate position as a hybrid of *C. p. pipiens* and *C. p. quinquefasciatus* with physiological characteristics of the former rather than the latter.

D. S. Bertram

VAN DER KUYP, E. **Mosquito Records of Aruba and Bonaire.** *Amer. J. Trop. Med.* 1948, Nov., v. 28, No. 6, 895–7, 1 fig.

Larvae and adults of the following mosquitoes were collected, between 1942 and 1947, during short visits to the islands of Aruba and Bonaire in the Caribbean Sea: *Aëdes aegypti, Culex quinquefasciatus,* [*C. fatigans*], *Psorophora confinnis* and *Deinocerites cancer.* A few larvae of *Uranotaenia lowi* were taken on Bonaire alone.

Oil companies began to operate in Aruba in 1927 and 1928, since when there has been large-scale immigration and the population has grown from 9,206 to 45,907 in 1947. Little is known regarding the incidence of mosquito-borne diseases in these islands. There seem to be neither anopheline mosquitoes nor malaria. Filariasis is very rare in Aruba but immigrants from endemic areas are present, together with the vector *C. quinquefasciatus.* In 1903 the last case of yellow fever was reported in Bonaire. *H. S. Leeson*

MUSPRATT, J. **Observation on the Larvae of Tree-Hole Breeding Culicini (Diptera: Culicidae) and Two of their Parasites.** *J. Entom. Soc. Southern Africa.* 1945, v. 8, 13–20, 5 figs. [15 refs.]

SIMIĆ, Č. & ŽIVKOVIĆ, V. Sur une nouvelle espèce de flébotome dans la Serbie méridionale. [**A New Species of** *Phlebotomus* **in Southern Serbia.**] *Acta Med. Iugoslavica.* 1947, v. 1, No. 3, 193–201, 6 figs.

UCHIDA, S. **Studies on the Biting-Lice (Mallophaga) of Japan and Adjacent Territories (Suborder Ischnocera Pt. I).** *Japanese Med. J.* 1948, Aug., v. 1, No. 4, 303–26, 8 figs.

THORP, J. M., DE MEILLON, B. & HARDY, F. **The Effect of 2 : 3-Dimercaptopropanol (British Anti-Lewisite) on the Toxicity of Neoarsphenamine for** *Ornithodorus moubata.* *S. African J. Med. Sci.* 1948, Oct., v. 13, No. 4, 151–8, 3 figs. [12 refs.]

DE MEILLON has previously investigated the possibility of administering substances to a mammal with a view to destroying blood-sucking insects which subsequently feed upon it [this *Bulletin*, 1947, v. 44, 469]. Organic arsenical compounds have some interest in this connexion. They are indeed toxic to the host, but that risk might be reduced by the use of BAL (British Anti-lewisite). It is known that compounds made between BAL and organic arsenicals are toxic to certain protozoa and it seems possible that they might also be insecticidal.

In the present work, neoarsphenamine (NAB) is administered intramuscularly to a rabbit. Ticks, *Ornithodorus moubata*, are fed on the rabbit and a blood sample for the estimation of arsenic is taken at the same time. As one may vary the dose of drug and the period between administration and feeding the ticks, they may be exposed to a very great range of dosage of arsenic. The amount of blood they take is estimated by weighing them before and after the feed. Extending their previous observations, the authors record the mortality of

ticks fed under a variety of conditions. They show that for a very wide range of values a linear relationship between the logarithm of the blood arsenic concentration and the mean reciprocal survival time of the ticks has been demonstrated. This was not altered by treatment of the rabbits with BAL.

P. A. Buxton

SVIRBELY, W. J., EARECKSON, W. M., MATSUDA, K., PICKARD, H. B., SOLET, I. S. & TUEMMLER, W. B. **Physical Properties of some Organic Insect Repellents.** *J. Amer. Chem. Soc.* 1949, Feb., v. 71, No. 2, 507–9.

See also p. 671, MOM, **El empleo de la protección antisolar y de los repelentes de insectos en los indigenas latinoamericanos.**

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

COLONIAL OFFICE. **Report on the Water Resources of the Bechuanaland Protectorate, Northern Rhodesia, the Nyasaland Protectorate, Tanganyika Territory, Kenya and the Uganda Protectorate** [DEBENHAM, F.]. Colonial Research Publications (No. 2). 85 pp., 3 diagrams, 18 maps (4 folding). 3 graphs & 24 figs. on 8 pls. 1948. London: H.M. Stationery Office. [10*s.* 6*d.*]

The scarcity of water throughout a great part of East and Central Africa is a matter of every-day knowledge. The astonishing feature of it is that by the standards of many other parts of the world the actual rainfall is quite adequate, and countries with no greater precipitation support dense flourishing populations, whereas in these parts of Africa population is restricted. The difference lies partially but not very greatly in an unsatisfactory annual distribution of rain in Africa, and very much more in a wasteful use of the land over centuries which has led to soil erosion, a quick run-off in the rains, and general aridity very soon after them. Ignorance of how to conserve water or even how to tap natural sources is a contributory factor to such an extent that Gillman, in a classic survey of population distribution, declared that the presence or absence of a permanent domestic water supply within the reach of primitive tools and skill determines the pattern of population.

Improvement in availability and use of water are more likely to benefit the African than almost any other measure and they are of direct medical and demographic interest. The author has surveyed the resources and made a series of recommendations, of which the most important is the promotion of small schemes of conservation on a village scale by such measures as the impounding of headwaters, the construction of wells, improvement of dambos (a form of swamp) and modification of springs, giving detailed examples of their working. He is to some extent concerned at the risk of increasing the prevalence of disease, particularly malaria, hookworm and bilharzia. The reviewer is naturally anxious that this should not happen, but as he sees the problem the usual alternatives are not healthy or unhealthy people, but people or no people, the new communities to be created by the measures now advised would not in any case start on a worse basis than those that now exist, and steps could readily be taken to improve their lot.

In the standard scheme for a village of 100 persons with 100 head of stock, the author considers that a daily supply of 1,500 gallons would be adequate, and that it could best be secured from a catchment area of 200 acres, collected in a small reservoir which would be controlled by a dam 200 feet long, 50 feet broad, 5 feet average and 12 feet maximum depth. This would be protected from direct access, and the water would be led through piping and channels to an appropriate water point. [The reviewer's reactions are that this is in

reality demanding very efficient conservation as such a community might often have little more than 300 or 400 acres at its disposal, and he would therefore like to have seen less emphasis in the report on the possibility of using makeshift piping and conduits which could only cause great wastage. For evidence that the scheme is in fact practicable in its broad outlines one can turn to the ancient irrigation works of Ceylon, some of which are now being revived, which by a great multiplication of works of this sort supported more people than do the countries now surveyed, despite the fact that the rainfall was about the same and the land available one fortieth of that now considered.]

G. Macdonald

SAUNDERS, I. G. **A Survey of Helminth and Protozoan Incidence in Man and Dogs at Fort Chipewyan, Alberta.** *J. Parasitology.* 1949, Feb., v. 35, No. 1, 31–4.

Fort Chipewyan is at the west end of Lake Athabasca, about 370 miles north of Edmonton, Alberta.

In the course of other investigations there during the summer of 1945, the author found evidence of human tapeworm infection and accordingly examined stools from as many persons as possible who had lived at least a year in the north. For practical reasons, most of those examined were children at the Mission School.

In all, 140 persons were examined by direct examination of a simple smear. The results included 4 specimens positive for *Entamoeba histolytica*, 10 for *Iodamoeba bütschlii*, and 19 *Giardia intestinalis*. No *Taenia* infections were found, nor were trematodes or *Ascaris*. No diagnostic facilities for *Enterobius* were available, though histories of many persons suggested its presence.

The only helminthic infection positively identified was *Diphyllobothrium latum*: ova were present in 16 of the 140 persons. Symptoms were few and vague and most of the infected persons were apparently unaware of their infection: no anaemia attributable to fish tapeworm was encountered. Eight persons were treated with castor oil and male fern, without evidence of toxicity.

The author discusses the factors affecting the incidence of *D. latum* infection in this area. The people are essentially nomadic, with " makeshift cooking conditions". This factor would not apply in the case of the children in the Mission School. It was possible to examine only 16 of the persons known to lead the nomadic life and 11 of these were positive for *D. latum*: indifference and suspicion made it difficult to obtain specimens from these people and even in the willing persons constipation, which is common, added a further complication.

The distribution of *D. latum* further north is discussed and from local information the author has reason to believe that the infection is " probably distributed all through the vast north country ".

It is also noted that 38 of 88 dogs examined harboured *D. latum*, but usually only a few ova were found. *Ancylostoma caninum* was found in 10 dogs and a cyst of *Isospora* (probably *bigemina*) in one.

[In connexion with the finding of *E. histolytica* in 4 human cases, the author writes: " Having no concentration or staining checks on the direct iodine smear observations, the author reports with some hesitancy the incidence of *E. histolytica* so much farther north than any previous records. It was a small-cyst race encountered occasionally in Saskatoon (Miller 1939), non-pathogenic, and was in Indians and half-breeds, not whites who might have been infected outside."] *H. J. O'D. Burke-Gaffney*

BOOK REVIEWS

MAURANO, Flávio & others. **Tratado de Leprologia.** [Treatise of Leprology.] **Vol. 1. História da lepra no Brasil e sua distribuição geográfica** [MAURANO, F.]. 206 pp., ill. **Vol. 2. Etio-patogenia e anatomia patológica** [ROTBERG, A. & BECHELLI, L. M.]. 451 pp., ill. **Vol. 3. Diagnóstico** [DE SOUZA LIMA, L. & DE SOUZA CAMPOS, N.]. 168 pp., ill. **Vol. 4. Clinica e terapêutica** [BECHELLI, L. M., ROTBERG, A. & MAURANO, F.]. 368 pp., ill. **Vol. 5. Epidemiologia e profilaxia** [DE SOUZA CAMPOS, N., BECHELLI, L. M. & ROTBERG, A.]. 397 pp., ill. 1944. Rio de Janeiro: Serviço Nacional de Lepra.

Several monographs on aspects of leprosy, written by well-known leprologists, have been issued by the Brazilian Health authorities. Now, at the instigation of the National Leprosy Service under the Director, Dr. Ernani Agricola, these writers have combined to produce a Treatise on Leprosy. This treatise consists of 5 volumes bound in two: 1. History of Leprosy in Brazil and its geographical distribution. The latter is dealt with again and more fully in Vol. 5. 2. Aetiology and Pathology. 3. Diagnosis. 4. Clinical description and Treatment. 5. Epidemiology and Prophylaxis.

Though published as long ago as 1944 this work must still be the most comprehensive in existence on this disease. The lack of comprehensive works in Portuguese and the difficulty of acquiring papers and books published abroad led, says the writer of the preface, to the preparation of the monographs referred to above, but in 1942 the decision was reached to combine in the form of a treatise the various articles for the information of medical men engaged with leprosy and its prophylaxis in all States of the Federation. So, in 1943, the National Leprosy Service was instigated to prepare four more sections (one on *Diagnosis, clinical, laboratory and biological* has already been issued in 1942) and to produce them complete in the form of a Treatise.

The work, though dealing primarily with conditions in Brazil, will be of enormous value to workers in any country where leprosy is rife. Thanks are due, therefore, to the Public Health Service of the Ministry of Education and Health in Brazil, under the Minister, Dr. Gustavo Campanema, and to the Institute of Inter-American relations of the United States. In the space at our disposal we can do little more than indicate the scope of this large work of nearly 1,600 pages.

Volume I, *History and Geographical Distribution*, is divided into 4 parts. Part I gives an account of the history of the disease and comprises three chapters. The first discusses the origin of leprosy in Brazil and states that it was not indigenous but was introduced by slaves from Africa and by the Portuguese from Europe; the second tells of the social and economic factors which caused the infection to spread over the country, especially by agency of the slaves; in the third the extension is described in more detail in each of the 22 constituent States of the Federation—a very interesting chapter tracing the increase from earliest times down to 1943. Part II also contains 3 chapters: one on the study of the disease in Brazil, started by Gomes in 1798; the second is a review of the epidemiology, treatment, the clinical aspect and pathology—merely a long list of names and dates; the third contains a short account of the spas reputed to be beneficial in treatment, and of vaunted charlatan remedies. Part III speaks of the habits and social customs of patients; mendicants, their isolation, hospitalization, segregation and the bans against them. Part IV deals first with official measures put into force in the colonial period, 17th to 19th centuries, then in imperial times to the present, with references to philanthropic and religious societies concerned with sufferers from leprosy. Following this is a sketch of scientific measures in the anti-leprosy campaign in the various

States and the co-operation between the State authorities and Societies for combating the disease. There is an appendix to this chapter, of documents of historical interest.

Volume I is interesting but is, naturally, not so full and detailed as Professor de Souza-Araujo's large and comprehensive work on the *History of Leprosy in Brazil*, two volumes of which have already appeared and have been reviewed in this *Bulletin* [1947, v. 44, 760; 1948, v. 45, 1132.]

Volume II, on *Aetiology and Pathogeny*, describes in 11 chapters the organism, its characters, the attempts at cultivation (this section is well illustrated), the relations between human and rat leprosy, the results of inoculation into rats, buffaloes, birds, opossum, cattle, sheep and horses, the possible hereditary or congenital transmission, the mode of penetration in man and its spread after gaining entrance, immunity and allergy, the lepromin reaction and the reactions to syphilitic antigen and to other acid-fast cultures, and the Witebsky-Klingenstein and Rubino reactions. Finally, accessory factors are considered, such as age, sex, nutrition, climate, other diseases and individual and racial predisposition. [Unless the editing of a large work such as this is very carefully done there is a danger of overlapping and repetition, and this last section is discussed again in the final volume of this treatise.]

The section on *Histopathology* comprises six chapters and is embellished with fine reproductions of photomicrographs of the tissue changes set up and in it are discussed the relations between the pathology and the clinical manifestations, the factors determining the mode of evolution and the course towards cure or death.

Volume III, on *Diagnosis*, is of the highest importance. The subject is treated from several aspects: (i) Clinical; the physical examination and the results of the histamine and pilocarpine tests. (ii) Bacteriological; the search for the organism in the nasal mucus, the skin lesions, the glands, the peripheral blood by thick drop and the Crow and the Rivas methods, the nerves and the secretions or excretions. (iii) Serological; the reactions of Rubino, Gomes, Lleras Acosta, Witebsky and others. (iv) Histological and Immunological, Mitsuda, Bargher, etc. Diagnosis of nervous leprosy is gone into in more detail and the differential diagnosis from syphilis, pityriasis, vitiligo, forms of eczema, various erythematous and achromic dermatoses. Tuberculoid and lepromatous types are similarly discussed. This section is well illustrated, some of the reactions being reproduced in colour.

Volume IV comprises two parts: 1. *Clinical*, 2. *Therapeutic*. The former is a splendid effort well carried out. All forms and aspects of the disease are described and depicted with excellent photographs, many coloured plates and with abundant references. Coloured plates showing the development of lesions of the nasal septum are remarkably good. The treatment section occupies less space, as is but natural since there is not very much to say on this subject. The treatment proper is prefaced by general remarks on appraising the results and warning against too ready acceptance of the *post ergo propter*, because good hygiene will bring benefit and the disease presents at times spontaneous remissions, so that amelioration after a certain treatment is not proof that the one is due to the other and the crucial test consists in observation of control cases, equal in number and stage and under similar conditions, untreated. Mention is made of treatment by improved general hygiene, by good food and properly balanced diet. Modes of treatment now little used are referred to: iodides, arsenicals, mercury, copper and gold salts, sera, vaccines, vitamins, sulphonamide drugs, diphtheria toxoid and antitoxin, carbonic acid snow, methylene blue, eosin and other dyes, phenol, thymol, guaiacol and several more. Lastly, in greater detail, chaulmoogra, the oil, the ethyl esters and fatty

acids. This book was published in 1944 (but received here only in 1949) and although Promin is mentioned, the remarkable results achieved in treatment by the Sulphones since that time are, of course, not mentioned. Special short chapters deal with treatment of the leprous reaction and the many drugs which have been tried for it ; of perforating and other forms of ulcer and the pain of the disease. The last few pages of this volume are given up to consideration of the part played by physiotherapy, mechanotherapy and hydrotherapy, including galvanism, high frequency, diathermy, U-V rays, heliotherapy, massage, physical exercises and gymnastics.

Volume V deals with *Epidemiology and Prevention*. Under the former heading are considered biological and social factors, climate, war, migration. The distribution and figures of prevalence based on censuses made in 1940 onwards and analyses of earlier records are given for the different States of Brazil, for South, Central and North America, Canada, the European nations, Asia and the Far East, Oceania, East, West and Central Africa, Egypt and the Sudan. Tables are presented to show the same more graphically. Other factors already referred to in Volume II, such as sex, age, occupation, race, climate, nutrition, general hygiene and sanitation, intercurrent disease, spread of infection in the family and factors favouring dissemination are all in turn debated, though some only briefly.

Lastly, Prophylaxis, in antiquity and in more recent times—periodic examination of contacts and associates, isolation, hospitalization, asylum-colonies, sanatoria, domiciliary segregation, rules for discharge, dispensaries for ambulant and probation patients, propaganda and educational measures, organization of a leprosy service, all come under discussion, ending with an account of the National Leprosy Service of Brazil and what it has succeeded in accomplishing and at what cost in each of the constituent States, the laws at present in force and additional laws proposed for adoption in the future.

The Minister of Health, the National Leprosy Service, the Editor and the contributing authors are all to be most heartily congratulated on accomplishing their huge task and producing a work which must surely be a standard of basic information for many years to come. Nor must we forget the producers and publishers. The whole set-up of the work is high class ; the print is clear and easy to read, the paper of a quality we have not seen for a long time in our own country, and the binding is neat and adequate. This work and Professor de Souza-Araujo's *Historia* will amply furnish all that anyone need know of leprosy.

H. Harold Scott

Agrícola, Ernani [Director do Serviço Nacional de Lepra]. **Campanha nacional contra a lepra.** [National Campaign against Leprosy.] Palestras proferidas ao microfone da PRA-2 do Serviço de Radiodifusao Educativa do Ministério da Educaçao e Saúde 7.xi.1944 a 16.viii.1945. 181 pp. 1946. Rio de Janeiro : Serviço Nacional de Lepra.

During the nine months, November 1944 and August 1945, Dr. Ernani Agrícola was directed by the Ministry of Education and Health of Brazil to deliver broadcasts almost every week, telling the people about leprosy and what was being done to deal with it in their own country. Thinking that these talks might be interesting and useful to a wider circle, the author has now collected them together and reissued them in a small book. From the point of view of the man in the street, including in this term the intelligent layman, these broadcasts would doubtless accomplish what they purport to do, for they are expressed in simple straightforward language, avoiding the use of technical terms.

They tell a little of the history of the disease in Brazil [among the authorities and authors mentioned we have failed to find the name of Professor de Souza-Araujo, probably the greatest authority in Brazil on this disease], and the following points are taken and spoken of in turn: Remarks on the epidemiology of leprosy and parallels between Brazil and other countries, such as India, Japan and the Philippines, the numbers of the afflicted, the numbers in special establishments and the types of these establishments, agricultural, asylums and hospital colonies. Several of these are referred to from time to time and the costs of their upkeep. Reasons are given for isolation and segregation and reference is made to various committees and societies for the relief of patients and their families, also to the methods for dealing with the children, for finding out concealed cases, for careful vigilance of patients to be discharged or kept under observation; for education of the people, propaganda and distribution of literature.

The broadcasts seem admirably adapted to their original purpose but, naturally, the detailed information is only of local interest and would not appeal in places outside Brazil. *H. Harold Scott*

DE SOUZA CAMPOS, Nelson & BECHELLI, Luiz Marino. **Sintomatologia nervosa da lepra.** [Symptomatology of the Nervous System in Leprosy.] 193 pp., numerous figs. on pls. Ministério da Educação e Saúde, Departamento Nacional de Saúde, Serviço Nacional de Lepra. 1946. Rio de Janeiro: Imprensa Nacional.

This is another of the series of excellent monographs dealing with different aspects of leprosy and issued by the Leprosy Section of the National Health Service of Brazil. This one deals with the nervous manifestations, the tests therefor and the general and differential diagnosis.

The thesis is divided into two main parts. In Part I are described and discussed in sequence the sensory changes, the motor disturbances and the trophic and vasomotor symptoms; in Part II, the clinical tests, the examination of patients, the actual condition and evolution of the nervous manifestations, the differential diagnosis and a summary or epitome of the neurological lesions and their classification. Apart from numerous footnotes in the text, there is appended a bibliography of more than 150 references. The statements made, it will be seen, are well documented. There are very clear diagrams shaded to show the distribution of lesions in certain patients and other very detailed, but clearly reproduced, figures to indicate the innervation of the muscles of the body and the roots from which the peripheral nerves arise, and another similar diagram of the cutaneous nerve supply. Photomicrographs demonstrate the histopathology of biopsy specimens of nerves and skin and, lastly, there are 59 photographs, direct and X-ray, to show the deformities and mutilations of the hands and feet and the bony changes produced by this disease.

To return to the letterpress: The methods of testing for the nervous symptoms are first detailed, the distribution of the anaesthesia and paraesthesias. This section is followed by a description of the motor disturbances in arms, legs and face, and this by a consideration of trophic changes in skin, subcutaneous tissues, muscles and bones and the mutilations resulting from absorption, dry gangrene and ulceration. In Part II, the clinical and laboratory examinations are discussed in greater detail, the histamine, pilocarpine and pricking tests and the methods of carrying them out; laboratory tests include examination for bacteria, the Mitsuda reaction and biopsy. Succeeding this chapter on methods comes a section on the various clinical signs and symptoms; the

anaesthetic zones, the neuritis, the amyotrophy and trophic lesions are described more fully.

The section dealing with the differential diagnosis of the nervous disturbances of leprosy from hysterical anaesthesia, from toxic neuritis, from syringomyelia and other conditions is most helpful ; some of these are expressed in tabular form in addition to being described in the text. The concluding section contains remarks on the classification of the nervous symptoms and lesions in leprosy and on the Cairo and American classifications of cases of the disease, showing the points of agreement and difference.

This monograph is well up to the high standard set by previous issues from the same authority, the Leprosy Service of the National Department of Health.

H. Harold Scott

DE SOUZA CAMPOS, Nelson & BECHELLI, Luiz Marino **Organização e Funcionamento de Preventórios.** [Organization and Management of Preventoria.] 128 pp., 42 figs. on 19 pls. & 1 diagram. Ministério da Educação e Saúde, Departamento Nacional de Saúde, Serviço Nacional de Lepra. 1948. Rio de Janeiro : Imprensa Nacional.

This is one of a series of monographs issued by the National Leprosy Service of Brazil. There seems to have been some delay in its publication, for it received the commendation of the Service in 1945, but the date of publication is 1948.

The book is difficult to review satisfactorily ; the question is studied from many aspects and the details are so numerous that careful reading and re-reading are necessary if we are to grasp the full importance of the subject. All aspects seem to have been considered : the advantages of preventoria, their planning, their pitfalls and their difficulties are frankly discussed. Hence the book is a valuable production, not only for Brazil, to which the work mainly applies, but to all countries where leprosy is rife.

In leprosy there are three necessary basic prophylactic measures, the hospital, the dispensary (*ambulatorio*) and the preventorium. It is not enough to isolate or segregate the infective, to treat and help him during an illness which may be prolonged ; his associates must be examined periodically to discover any in an early stage of infection when treatment can be availing and before the person himself becomes infective and when segregation is not necessary or advisable.

The organization and management of a preventorium is not a simple matter ; there must be a medical division, a paediatric section, a dermatologist and leprologist, a dentist, an ear, nose and throat specialist and an ophthalmologist, apart from a caterer and dietitian, and persons to see to social and educational aspects—the last being of the highest importance for young children.

The book is divided into three parts, each with subsidiary chapters. Part I is concerned with general questions and comprises four chapters. The first takes up the matter of the child of leprous parents, whether infection is transmitted hereditarily, germinally or congenitally, and gives reports from writers in different parts of the world—Brazil, Mexico, India, Japan, the Philippines, Basutoland, Rumania, Norway. Documentation in this respect is very full ; in a short paper of 14 pages there are more than 100 references in footnotes. The second chapter considers the rôle of the preventorium in leprosy prophylaxis, the care of the children and their education until they reach an age when they can go out, mix with the world and make their own way. Hospital, Dispensaries and Preventorium make a natural triad ; hospitals receiving infective patients and sending out those no longer infective ; dispensaries looking after the latter,

returning them to hospital if necessary, or relegating them to preventoria which, in turn, receive the newly-born and young children sent in by the inspector and, according to developments, retains them, discharges them or sends them to hospital. Chapter III is historical, giving a sketch of the rise and development of preventoria, based largely on Professor de Souza-Araujo's great works " Leprosy in Forty Countries " and " The History of Leprosy in Brazil " [see this *Bulletin*, 1947, v. 44, 760 ; 1948, v. 45, 1132] ; starting from Father Damien's establishment on Molokai in 1880, the authors tell of what was done in Colombia, in the Argentine, in Trinidad, in Nigeria and in Brazil. In Brazil there are now 27 preventoria in 22 States ; Minas Gerais has four, Pará and São Paulo two each. The last chapter of this section discusses the co-operation between official or governmental services and private associations.

In Part II, the authors deal with what they call the Static part of preventoria, by which they imply the localization and organizational plans of them. These are dealt with in two short chapters of 3 pages each. The first is given up to the vexed question of localization, whether they should be near the leper hospital or at a distance, whether within the town's boundaries or outside. If near the hospital administration is facilitated, but separation of one from the other is difficult and the risk of infection is greater, unless there is constant vigilance to ensure compliance with rules. It is better to have them situated in an urban area because, it must be remembered, the inmates are essentially healthy individuals, but they should be within easy reach of medical attention and able to benefit from social amenities. The stigma of " children of lepers " is fast becoming obliterated.

The planning of a preventorium will naturally depend on the number of inmates to be received or provided for. There must be an administration block, a crèche, dormitories, recreation rooms, sick-rooms, a room for older inmates from 12–20 years of age, a solarium, bathrooms, lavatories, etc.

Part III is designated the Dynamic Aspect of Preventoria and is concerned with internal administration, cost of upkeep, questions of admission and discharge, the way of life of the inmates, the clinical aspects of infantile leprosy, the results of the lepromin reaction and the chances of studying certain phases of the disease, and research into the initial stages. This part is much the longest and makes up three-fifths of the whole book. The Federation has adopted and promulgated a list of over 50 rules, or articles, each of which is detailed. Other chapters discuss the conditions justifying, and the criteria to be adhered to in respect of, admission of children of leprous patients, of children sent in by regional service officers and travelling dispensaries, the use of the lepromin reaction before allowing inmates to leave. Life in the preventoria is described, the food, gymnastics, games, education both secular and religious, medical and dental care. There is an excellent photograph of happy infants, two, three and even four in one bassinette out in the sunshine, and another of older children apparently being instructed in physical drill.

As regards leprosy research, the preventorium offers facilities for study of the epidemiology and family relations of the disease, of the early manifestations, the evolution of incipient infection and the lepromin reaction. The early lesions considered are the hypochromic and achromic, the erythematous and tuberculoid lesions. Some of these are illustrated by photographs. Those characteristic of infancy are stated to be the tuberoid, papular and lichenoid ; in older children and adults Boeck's sarcoid and trichophytoid or annular lesions.

The final chapter describes Mitsuda's lepromin reaction and its interpretation. In addition to the footnote references mentioned under chapter I, there is appended a bibliography of over 100 titles. *H. Harold Scott*

GUIJA MORALES, E. [Catedrático de medicina legal, Médico-director del Hospital Psiquiátrico Provincial de Cádiz]. **Psicosis palúdicas y atebrínicas. Trastornos psíquicos en el paludismo espontáneo, en el terapéutico y en los tratamientos con preparados atebrínicos.** [Psychic Disturbances in Malaria, Spontaneous and Therapeutic, and in Treatment with Preparations of Atebrin.] pp. ix+173, 3 charts. Colección de Monografías de Investigaciones Médicas. 1945. Barcelona: J. M. Massó.

This is one of a series of medical monographs by Spanish authors of repute, edited by J. M. Massó of Barcelona. In the present instance the author's first idea was to deal with the last only of the matters mentioned in the title, as he had seen several cases among patients treated with atebrin [mepacrine], but later it was deemed advisable to enlarge the scope to include similar disturbances occurring in ordinary untreated malaria subjects and in patients undergoing therapeutic malaria treatment.

The study was begun in Cáceres, where malaria is endemic, and continued in Cádiz. Before undertaking a description of *malarial* psychoses, the author thought it would be wise to give a brief account of common psychoses, which he designates " symptomatic psychoses," apart from the malarial forms. The whole work is, therefore, divided into four chapters: 1. Symptomatic psychoses, as met with in everyday clinical psychiatry. 2. Psychic disturbances in malaria, " spontaneous malaria " as the author calls it. 3. Psychic disturbances occurring in patients undergoing therapeutic malarial treatment. 4. Psychic disturbances among patients treated by atebrin preparations.

In chapter I he gives a brief account of psychic disorders which he subdivides into two main groups: those primarily cerebral or organic, and those with functional toxic effects on the central nervous system. Under the latter are included disorders due to poisons *ab extra*, as alcohol, morphine and lead, and those occasioned by disease such as infections, endocrine disturbances, etc. It is to the latter that the author restricts the term symptomatic psychoses. [Not a very satisfying classification, because " organic " causes will interfere with normal function, and, on the other hand, toxic effects may not be purely " functional", but may lead to definite lesions.] In this connexion the author refers to such conditions as hebetude, mental confusion, anxiety, outbursts of anger and of threats, of delirium, incoherence, mental perplexity, stupor, depression and hallucinations; after the fever has subsided there may be post-febrile psychoses, as emotional upsets, irritability, " emotional hyperaesthesia ", depression and hypochondria, impairment, perhaps loss, of memory.

The malarial psychoses, chapter II, come to the notice of clinicians and malariologists more often than to that of psychiatrists. They are usually abrupt in onset and are seen as confusional states, " patchy " forgetfulness, exhaustion, hallucinations, perhaps coma, or sudden mania, melancholia, Korsakov's symptom; these usually accompany the febrile stage. In chronic malaria we see cases of depression and melancholia, or apathy and indifference. Paranoia is not uncommon, especially, says the author, in tropical countries. It is not easy to differentiate organic malarial encephalopathy from psychoses not due to actual cerebral lesion. [Perhaps there is no real distinction, and the latter—extra-nervous psychosis—may be associated with cerebral lesions not yet discovered.] The symptoms may be due to vascular embolism or thrombosis, to punctiform haemorrhages, with sudden loss of consciousness and, especially in children, with convulsions. Other conditions have been reported, such as monoplegias, trismus, Parkinsonism, chorea, amaurosis, epileptic attacks and bulbar symptoms.

The author concludes that he can distinguish 7 clinical types: 1. That caused by malarial encephalopathy. 2. Symptomatic malarial psychosis due to the

physical action of the infection on the central nervous system. 3. Symptomatic malarial psychosis proper. 4. Endogenous psychosis in the course of a malarial attack. 5. Abnormal psychic reaction provoked by the infection. 6. Psychic symptoms attributed to malaria, but feigned by the patient as an interested person. 7. Psychic disturbances of a non-malarial nature, but coinciding with a malarial infection. [To the reviewer these seem somewhat artificial and not easily differentiated, with exception of type 6.]

Therapeutic malaria, chapter III, has afforded an opportunity for observing certain types of psychosis produced by the action of malaria on different personalities, in particular general paralytics. These cannot be ascribed solely to the malaria because some of them at least may be observed in patients with general paralysis treated with other pyrogenics, or even drugs such as neosalvarsan. The following are specially referred to in this chapter :

1. Paranoiacs with hallucinations (the so-called Gerstmann psychosis), or the schizophrenic. The hallucinations are most commonly auditory, next visual or tactile, more rarely of taste or smell. They are seen oftenest in the last days of the induced fever, or after treatment of the malaria, and it may be some time after. Records show that 5–18 per cent. of patients exhibit this form. The case is quoted of a man of 45 years who at each access of fever became very excited, attempted to tear his clothes and to hurl himself through the window, would break every thermometer he used and, in the apyretic intervals, had auditory and visual hallucinations. Under treatment by quinine the psychosis disappeared ten days after the temperature became normal.

2. Suicidal tendencies. The author differentiates those who attempt, and even commit, suicide owing to depression from their disease, before, during, or after treatment by malaria, and those who do so in the stage of depression after the course of malaria.

3. Cases in which the patient does not react in the usual way to the malarial infection. One case is recorded where the patient developed fever of a typhoid character after inoculation with the subtertian parasite and died in 10 days ; in another patient general depression, a rapid pulse, diarrhoea and uraemic symptoms necessitated stopping the treatment at the third access of fever.

4. Decline of the general paralysis symptoms, reversible or not, with psychosis. One patient after the 6th access of fever stayed motionless, neither speaking nor appearing to understand anything, with uncontrolled sphincters ; he had to be fed by tube. The treatment was stopped at the 10th access of fever. Six days later he had troublesome visual hallucinations ; on the 10th he regained control of his sphincters, but convalescence was prolonged for two months.

5. Epilepsy following malarial therapy.

Chapter IV quotes reports of many cases of psychosis in the course of treatment of malaria by atebrin and repeats Kingsbury's explanation that the atebrin, by destroying the parasites more rapidly than does quinine, liberates a flood of toxin which causes the symptoms, or the atebrin has a direct toxic effect on the central nervous system.

The author sent a questionary to the doctors of Cáceres and Cádiz, asking them how many malaria patients they had had in the preceding five years, how many had been treated with atebrin (or atepe), in how many of these they had observed psychic symptoms, and to give details. He then quotes cases : one with a manic-depressive state ; another with sudden delirium, incoherence and insomnia (but several members of this man's family—uncle, father and sister—exhibited symptomatic psychosis) ; another had vomiting

and diarrhoea and complained that she was being poisoned and she refused all food, and at other times appeared perplexed and constantly asked what was happening. These symptoms did not occur when quinine was given, but only after atebrin. Other similar cases are noted.

The author then made some experiments, administering atebrin to healthy persons to see if psychoses were set up in any of them. He gave to each "5–8 tablets" of atebrin (or atepe) daily for a week but, though signs of intolerance, such as vomiting, might be seen, none showed any psychosis. He then gave the drug intramuscularly, the contents of an ampoule of 0·3 gm. of the hydrochloride. One subject on the fourth day became confused, kept looking under his bed to see if anyone was hiding there and on leaving his room he seemed unable to recognize it on his return and went into others, or he would remain motionless and mute, or repeatedly say "Pardon me, pardon me; say it again." This condition persisted for 16 days. The author concludes that atebrin *can* cause psychosis in man. This, however, was the only one among several who received the atebrin inoculation, and the inference is drawn that there must be some susceptibility or tendency to psychosis also playing a part.

Analysing 34 cases the author finds that as regards:

1. *Sex.*—Nineteen were males, 15 were females—a difference of no moment.

2. *Age.*—Twenty-one were between 9 and 23 years (years of puberty and adolescence), two only between 24 and 40 years; 8 were in the fifth decade, and there was only one over 50 years [this totals 32].

3. *Others in family.*—Eighteen gave a history of "psychic pathology" in close relations, parents, uncles, cousins.

4. *Dosage of atebrin* which preceded the psychosis. Thirteen had the usual dose of 3/7 (3 tablets daily for 7 days); 13 others had less than this, 2/1 to 3/6; 7 had higher doses, from 13/1 to 3/15.

5. *Stage of treatment when the psychosis was observed.*—Thirteen showed symptoms during the course, while in 20 the course was completed, or they were given a larger dose. In 11 of the 13 symptoms appeared after the ordinary dose of 3/7, with an interval up to 48 hours; in the other two the interval was longer, 9 and 18 days.

6. *Course and termination of atebrin psychoses.*—The commonest early symptom was mania with confusion and when this is all the prognosis is good, as the symptoms clear in a few days, except for some restlessness and insomnia. Those with other complications clear up more slowly, but all the author's patients recovered in time without any residual psychotic change. In four only were the symptoms prolonged over a month, in 27 they lasted "from a few hours to one month."

Summing up, the author states that atebrin psychoses occur in 2–5 per thousand cases. In making a diagnosis it is far from easy to exclude endogenous psychosis and abnormal psychic reactions. With psychosis in untreated malaria we find parasites in the blood, whereas in atebrin psychosis we should not. On the other hand, this is not all, for a malarial psychosis may persist after the infection has been eradicated.

The subject bristles with difficulties and the distinction between ordinary psychoses and those due to malaria or to atebrin is not so easy in practice as it may be made to appear on paper. The author is, however, to be congratulated on the accomplishment of a difficult task and on having provided a basis for future work on a vexed question. [See also FINDLAY, this *Bulletin*, 1947, v. 44, 763.] *H. Harold Scott*

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